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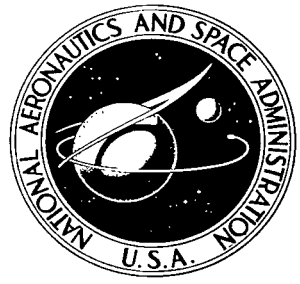

PROBLEMS OF SPACE BIOLOGY, VOL. 10

Nerve Mechanisms of Vestibular Reactions

by A. N. Razumeyev and A. A. Shipov

"Nauka" Press, Moscow, 1969

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NERVE MECHANISMS OF VESTIBULAR REACTIONS

A. N. Razumeyev and A. A. Shipov

This book summarizes the achievements in recent years in the electrophysiological investigations of specific links of conducting paths of the vestibular analyzer, its interaction with stimuli, character of impulses arising in the receptor, and the characteristics of their conduction along the vestibular tract. /4*

A significant place is given to questions of the m thematical description of the functioning principles of peripheral portions of the vestibular analyzer, to the stimulation of the activities of the oculomotor apparatus, to the mathematical treatment of rhythmic changes of neurons in various regions of the cortex and subcortical formations of the brain with adequate stimulation of the vestibular apparatus.

The book relied upon the scientific research of physiologists, otolaryngologist-doctors and engineers, occupied with the questions of the stimulation of physiological functions.

*Numbers in the margin indicate pagination in the foreign text.

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"Nature is not aware of our divisions of sciences. It is one. This signifies, that a true knowledge of her laws demands the collective efforts of many sciences; otherwise we will see only one side of the phenomena and know nothing of the other..." /5

Academician N. Semenov
(Nauka i zhizn', No. 1, p. 3, 1968)

FOREWORD

The interaction of analyzers responsible for spatial orientation, formation of posture and motor acts, suffers noticeable changes under the conditions of weightlessness. Biological experiments on rockets, and then investigations carried out on human beings on airplanes describing Kepler parabolas, and, finally, astronaut flights turned attention to the special significance of the vestibular analyzer. The practice of space flights put before physiology the task of explaining the mechanism of vestibular disorders observed under the conditions of weightlessness.

A solution to the question, however, is complicated by the obvious insufficiency of knowledge in relation to the function of the vestibular analyzer and the interaction of its separate parts.

Nonetheless, in recent years in the USSR and abroad, a large quantity of work has appeared which is dedicated to the study of the functional characteristics of the vestibular analyzer.

The book of our colleagues and students, A. N. Razumeyev and A. A. Shipov, gives a generalization of the achievements of recent years on electrophysiological investigations of specific groups of conducting paths of the vestibular organizer, the interaction of its parts, the character of impulses arising in the receptor, characteristic of their conduction along the vestibular tract, and also of questions of the mathematical description of the functioning of peripheral sections of the vestibular analyzer.

In this book questions of biophysics and physiology of the vestibular receptors are examined, as are the reactions of neurons of various sections of the vestibular analyzer with adequate and inadequate stimulation of the labyrinth, functional connections both inside the vestibular analyzer as well as with other analyzers. Descriptions are cited of the methodological experimental methods with the application of contemporary mathematical methods of /6

treating experimental materials.

This book is of interest for a wide range of scientific researchers and doctors, and also for cybernetic engineers.

Academician V. V. Parin
O. G. Gazenko, Corresponding Member, Academy of Sciences USSR

CHAPTER I

FUNCTIONAL MORPHOLOGY, BIOPHYSICS AND PHYSIOLOGY OF VESTIBULAR RECEPTORS

Functional Morphology

Concise Information of Phylogenesis, Ontogenesis and Anatomy of the Internal Ear

The organ of hearing and balance is a membranous labyrinth /7
appearing as a system of thin-walled sacs and ducts, filled with a fluid endolymph. This system is closed in a petrous bone, the space of which is only partially filled with the membrane labyrinth. The membranous labyrinth is situated as if it were suspended in the perilymphatic space by means of a number of connective tissue lacerti (lacertus fibrosis), passing through the internal surface (endosteum) of the bony labyrinth and the connective tissue membrane of the membranous labyrinth.

All vertebrate animals: fish, amphibians, reptiles, birds and mammals have principally the same labyrinth structure, although differences in its concrete embodiment are as numerous as are the types of animals.

The labyrinth of vertebrates is situated symmetrically in the right and left halves of the skull and is represented by the utriculus, sacculus and lagena (in evolutionary development, this disappears when the cochlea completely develops) with maculae and otoliths; the macula neglecta (which is lost in the majority of mammals, except for the mole and the squirrel); by a system of semicircular canals with crests and cupulas; and by a cochlea with Corti's organs (Fig. 1).

Thus in a more developed form the internal ear appears as a sensory organ with three purposes. There are receptors of angular acceleration (semicircular canals), of linear acceleration including gravitational acceleration (otolithic organs), and an organ for the precise frequency analysis of sound (Corti's organs of the cochlea) in the ear.

It is assumed (by Pumphrey, 1950; Lowenstein, 1960 and others)

that the history of the development of the internal ear in vertebrates begins with the lateral line organ. Even at the present time several fish have in their integument hair cells which evidently are none other than indicators of water currents. There is /8
every basis for viewing such kinds of cells as the original organ of spatial orientation. Further in the process of evolution, these cells were imbedded in systems of subepidermal tubes and evolved into lateral line organs. Insofar as aquatic animals have approximately the same density and compressibility as the medium they inhabit, then any body moving in the water will deform the surface of the animal just as if it were directly touching it. Thus objects moving nearby are discovered with a certain precision simply by a determination of the points of maximum pressure. Inasmuch as the calcium content in seawater is very high, at a certain stage of evolution a deposit of calcium carbonate ($CaCo_3$) could be formed, giving rise to otoliths. But in such a case the lateral line organ had to become sensitive not only to stimuli which were adequate for unloaded organs (vibrations), but also for deformations caused by gravitation (linear acceleration). There are no fish with a loaded lateral line organ. This is not surprising since, as a result of further evolution, there was an isolation of the labyrinth and a division of the perception of enumerated classes of stimuli between its separate organs. /9

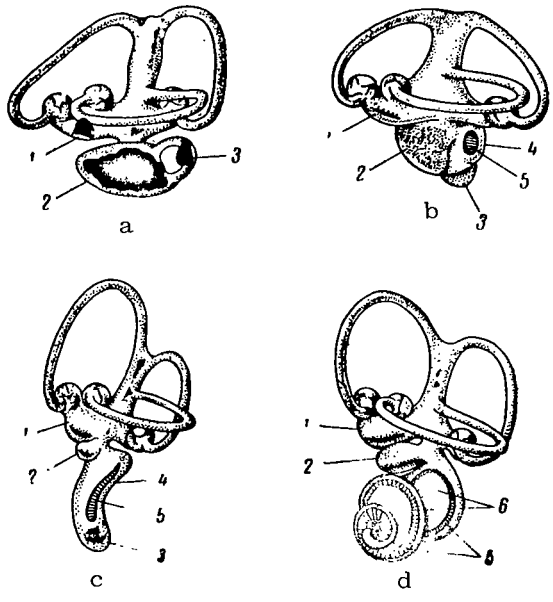

Fig. 1. Labyrinths of Various Vertebrates: (A) Fish; (B) Turtles (C) Birds; (D) Mammals; (Prosser, Braun, 1967).
(1) Utriculus; (2) Sacculus; (3) Lagena; (4) Auditory Papilla; (5) Basilar Membrane; (6) Cochlea.

The labyrinth was enclosed and a single connection with the external medium remained, i.e. the ductus endolymphaticus, so that the terminal organ proved to be completely protected from the external liquid current. The terminal organs of the semicircular canals either lost otoliths or the cupula did not have them at all, and the very same semicircular canals acquired a structure which enabled them to become sensitive only to angular accelerations. The necessity of separating sound and gravitation lead to the development of a cochlea with Corti's organ (Pumphrey, 1950).

The Semicircular Canals

The three semicircular canals (a complex of one side of the skull) are distributed in planes which approximately form a right-angle coordinate system. Very often a canal does not have the correct round form, and moreover it bulges out of its own plane, then re-enters it; but on the average each canal can be associated with a definite plane. The circular shape does not at all appear essential for its function, since there is no necessity for the canal to be ideally uniform. Each canal exits from a common cavity (utriculus) and describing an arc close to a hemisphere returns to it from the opposite side (Fig. 1). In direct propinquity to the utriculus the canal expands sharply, by ten times (Dohlman, 1935), forming an ampulla, and then again contracts to the basic diameter on the order of 0.3 mm, is opened into the utriculus. In the ampulla a receptor structure is located - a sensory crest with a neuroepithelium consisting of epitheleal sensory cells, the filiform processes which penetrate the canaliculus (3-5 μ in diameter) of the jelly-like cup - the cupula (Fig. 2). The cupula is a mobile structure having approximately the shape of a citrus section (Groen, 1956). Between the crista and the cupula there is a thin (2-5 μ) fluid layer - the subcupular space, which gives the possibility for the cupula to move along the crista as if on a hinge, thereby deforming the hairs of the sensory cells. The cupula closely adjoins the ampulla, and insofar as the semicircular canals (and also the utriculus, sacculus, lagena and cochlea) are filled with a fluid (endolymph), then the fluid ring of canals will bend and shift the cupula along the crest as soon as the endolymph comes into motion under the influence of inertial forces. The density of the substance of the cupula is the same as that of the endolymph; also the coefficients of refraction are identical; hence the living cupula is invisible in the ampulla, and only staining the endolymph with India ink reveals its presence in the form of a white silhouette. The motion of the cupula is rigidly connected with the motion of the endolymph in the canal, and neither gravitational nor centrifugal forces can shift or bend /10
this delicate instrument (cf. Chapter II). From a functional point of view, the shape of the crista is very interesting (Dohlman, 1961). The human crista in cross section has a half-moon shape, "the horns" of which come to half the circumference of the circular space of the ampulla. Turning attention to the fact that the cupula, filling this ampullar space, is united with the canals and utricular inclinations of the crista, it is possible to assert that the true shape of the cupula in cross section is elliptical, whereby the larger axis of the ellipse is directed from the base of the crista to the ampullar vault. Cross sections of the horizontal and vertical ampullar canals do not differ from one another. In man the only difference from the animals is that the crista of the vertical canals is oriented perpendicular to the

plane of the canal, and the crista of a horizontal canals is at a certain angle. Moreover, in animals there is a fundamental difference between cristae. The cristae of the phylogenetically older vertical canals make contact with the ampullar wall by a formation of two planum semilunatum, whereas the cristae of the phylogenetically younger horizontal canals are simple asymmetrical formations (Mygind, 1948).

Do the lateral portions of the cristae have any kind of sensory epithelium and innervation which could be compared to the innervation of the central portions of the crista, which is always viewed as the more significant, if not the only, surface important for stimulation of the hair cells?

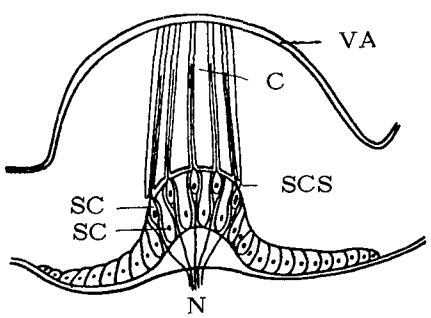

Fig. 2. Structural Scheme of the Ampullar Organ (Longitudinal Section of the Ampulla with the Cupula and Crista) (Groen, 1956).
VA - Vault of the Ampulla; C - Cupula; SCS - Subcupular Space; SC - Sensory Cells; SC - Supportive Cells; N - Nerve.

Histological preparations of cross sections of cristae of the shark, frog, alligator, cat, pigeon and monkey gave a picture of the nerve fiber distribution along the sensory epithelium. In the first place, it is well known that the nerve system of both vertical canals is separated into two branches and that the horizontal ampulla is innervated with a single nerve. The peripheral edges of the crista of the vertical canals in the lower animals receive almost all nerve fibers, whereas comparatively few fibers go to the central portion of the crista. In the second place, in the horizontal canal the dilation of /11 the crista and its flabellate expansion to the lateral wall of the ampulla is innervated by a larger bundle of nerve fibers, but only a small ramulus approaches the opposite medial side of the ampulla, which is clearly visible on the labyrinth of the pigeon.

The explanation for such a distribution of nerve fibers (in lateral sections) could be either that the lateral portions possess a larger surface of sensory epithelium than the central part, or that the sensory epithelium of these regions requires a denser innervation for each hair cell.

In order to investigate this problem, the surface of the sensory epithelium was measured and the quantity of nerve fibers in various portions of the crest on preparations of cross sections

of the nerve and the crest were calculated (Dohlman, 1961).

The number and probably the density of myelin nerve fibers was greater in the lateral portions than in the central portions. If the nerves of the reticular canals in man were not separated into two branches, as in the lower branches, and even if the nerve fibers in ampullar cristae were distributed in a more random fashion along the sensory surfaces in all ampullas, then the principle of intensified innervation and relatively greater sensory surface of the lateral portions of the crista and the flabellate distribution of fibers along the lateral walls is probably a general principle in many types of animals including man.

With the motion of the endolymph the cupula not only bends, but also slides along the surface of the sensory epithelium, which can be observed in experiments with the injection of India ink into the endolymph (Vilstrup, 1950 a, b, c; Dohlman, 1961). The fact that the central portion of the cupula moves far down along the canal and utricular inclinations of the crista indicates that the center of revolution of the cupula is located in the lower portion of the crista. From a mechanical point of view, the central part of the cupula, consequently, is a long lever from a fulcrum on the inclination of the crista to the vault of the ampulla. Since the lateral portions of the sensory epithelium are distributed to the middle of the lateral portions of the ampulla (in man), then with rotation of the lever the lateral portions of the cupula will cover distances along the sensory epithelium greater than those crossed by the central portions of the cupula.

The size of the path traversed by the lateral portions will depend upon the force acting upon the cupula and upon the elastic characteristics of the cupular structure. Such a mechanical structure is well adapted for the cupula to make slipping movements along the important sensory regions of the lateral walls of the ampulla, even with small displacements of endolymph.

In contrast to the great variation in body sizes, the semicircular canals of various animals are approximately alike in size. Jones and Spells (1963) measured the internal radius (r) and the radius of curvature (R) of the semicircular canals of 87 types of animals, including 46 mammals, 17 birds, 17 fish and 7 reptiles, according to available models and photographs.

TABLE 1

SIZES OF THE SEMICIRCULAR CANALS OF VARIOUS ANIMALS /12

(Jones, Spells, 1963)

Form	Average Mass, kg	Internal Radius (r), mm	r^2, mm^2	Radius of Curvature (R), mm	Volume of the Ampula (V), mm^3	$\frac{r^2R}{V}$
Mammals						
Man	70	0.14	0.0195	3.15	--	--
	--	0.13	0.017	3.4	--	--
Yellow baboon	14	0.115	0.013	2.7	1.0	0.0355
Black orangutan	13.5	0.155	0.024	2.55	1.75	0.035
Green marmoset	5.25	0.125	0.0155	2.8	1.65	0.026
Hocheur monkey	5.35	0.165	0.027	3.0	2.75	0.0295
Marmoset	0.26	0.135	0.018	1.95	0.86	0.0415
Madagascar lemur	1.3	0.090	0.0081	2.0	--	--
Loris	0.53	0.115	0.013	1.7	0.40	0.055
Fruit-eating bat	0.42	0.080	0.0064	1.5	0.335	0.055
	--	0.135	0.018	1.9	--	--
Tiger	155	0.165	0.027	3.4	--	--
	--	0.14	0.0195	2.8	--	--
Dog	14	0.135	0.018	2.4	--	--
	--	0.175	0.0305	2.1	--	--
Land wolf	42	0.13	0.017	2.35	0.755	0.0525
Mongoose	2.5	0.11	0.012	1.5	0.505	0.0355
Otter	12	0.080	0.0064	1.95	0.365	0.034
Weasel	0.084	0.080	0.0064	1.2	--	--
Raccoon	4.05	0.12	0.0145	2.55	--	--
Fur seal	64.5	0.19	0.036	4.4	--	--
Black seal	170	0.16	0.0255	4.3	--	--
Sea lion	20.5	0.12	0.0145	2.2	--	--
Chamois	150	0.19	0.036	3.7	2.85	0.0465
Gazelle	24.5	0.155	0.024	2.95	2.75	0.019
Sheep	48	0.1	0.01	2.7	1.7	0.0155
Arabic camel	455	0.14	0.0195	3.1	--	--
Pig	105	0.16	0.0255	2.9	2.4	0.027
Horse	450	0.195	0.038	4.1	3.55	0.044
3-toed sloth	3.1	0.12	0.0145	1.7	0.385	0.064
Anteater	3.9	0.12	0.0145	21	--	--
Hare	1.75	0.090	0.0081	2.15	--	--
Rat	0.21	0.090	0.0081	1.4	--	--
Jerboa	0.044	0.1	0.01	1.75	0.3	0.0585
Rabbit	0.44	0.11	0.012	2.2	--	--

TABLE 1 (Continued)

/13

Form	Average Mass, kg	Internal Radius (r), mm	r^2, mm^2	Radius of Curvature (R), mm	Volume of the Ampula (V), mm^3	$\frac{r^2R}{V}$
Guinea pig	0.25	0.105	0.011	1.9	--	--
Squirrel	0.2	0.08	0.0064	1.6	0.26	0.039
Porpoise	25	0.155	0.024	3	1.1	0.066
Porcupine	0.51	0.12	0.0145	1.15	--	--
Porcupine	--	--	--	1.7	--	--
Mole	0.034	0.08	0.0064	1.3	0.08	0.105
Dolphin	50	0.095	0.009	0.87	--	--
Dugong	230	0.16	0.0255	3.4	1.25	0.0685
Bonytailed kangaroo	22.5	0.1	0.01	1.9	0.355	0.0535
Blackfaced kangaroo	19	0.125	0.0155	2.85	0.735	0.0605
Vulpine phalanger	2.1	0.305	0.0105	1.85	0.455	0.0435
Marsupial mole	0.25	0.077	0.0059	0.95	--	--
Kangaroo rat	0.07	0.08	0.0064	0.94	0.14	0.0435
Marsupial rat	0.025	0.075	0.0056	1.15	0.16	0.004
Shortnosed bandicoot	1.05	0.07	0.0049	1.2	0.17	0.035
Platypus	0.57	0.115	0.013	1.9	--	--
Birds						
African ostrich	120	0.24	0.0575	3.85	4.1	0.0545
Kiwi	--	--	--	--	4.8	0.046
Red cropped loon	1.6	0.1	0.01	1.75	0.895	0.02
South African cormorant	2.25	0.18	0.0325	3.1	1.6	0.063
Great South African cormorant	3.95	0.19	0.03	3.55	1.55	0.0825
Night heron	2.25	0.14	0.0195	2.65	2.1	0.0245
Duck	13	0.14	0.0195	2.3	--	--
The same	0.98	0.11	0.012	2	--	--
The same	--	0.14	0.0195	2.6	--	--
Kanyuk*	0.72	0.23	0.053	3.4	2.3	0.0775
Greater tinamou	0.75	0.125	0.0155	1.95	0.72	0.0425
Hen	1.6	0.145	0.021	2.9	0.84	0.0725
Reed partridge	10.5	0.16	0.0255	2.35	--	--
Monarch crane	6.8	0.19	0.036	3.2	2.05	0.056
Pigeon	0.67	0.15	0.0225	2.95	0.585	0.115
Cockatoo	0.8	0.14	0.0195	3.2	1.6	0.039
Rabbit owl	0.54	0.19	0.036	2.9	1.9	0.054
Grey crow	0.44	0.14	0.0195	2.8	1.4	0.0385
Singing thrush	0.062	0.115	0.013	1.9	0.545	0.046

* Similar to a hawk.

TABLE 1 (continued)

/14

Form	Average Mass, kg	Internal Radius (r), mm	r^2, mm^2	Radius of Curvature (R), mm	Volume of the Ampula (V), mm^3	$\frac{r^2R}{V}$
Reptiles						
Giant tortoise	200	0.21	0.044	1.8	--	--
Gecco	0.014	0.13	0.017	1.4	--	--
Spotted lizard	0.485	0.14	0.0195	3.35	--	--
Blunt-tailed skink	0.415	0.14	0.0195	2.7	--	--
West African python	6.15	0.15	0.0225	2.6	0.395	0.15
Giant toad	0.26	0.14	0.0195	1.4	--	--
	0.33	0.1	0.01	1.25	--	--
Fish						
Roach	0.34	0.16	0.0255	3.2	--	--
Tench	0.45	0.19	0.036	3.2	--	--
Trout	0.23	0.155	0.024	5.1	--	--
Tunny	135	0.195	0.038	11	--	--
Hake	2.05	0.185	0.034	6.2	--	--
Perch	0.17	0.2	0.029	4.5	--	--
	--	0.14(H)				
	--	0.18				
Chimera	0.91	0.315	0.0755	5.7	--	--
	--	0.24 (H)				
	--	0.285				
Mol'va	0.43	0.36	0.093	7.8	--	--
	--	0.25 (H)				
	--	0.325				
Brama	0.45	0.17	0.0255	4.3	--	--
	--	0.15 (H)				
	--	0.185				
Sea tongue	0.34	0.19	0.034	3.7	--	--
	--	0.18 (H)				
	--	0.185				
Scomber	1.25	0.18	0.0325	3.3	--	--
Blackcrusted halibut	4.05	0.3	0.0675	4.9	--	--
	--	0.22 (H)				
	--	0.275				
Sea eel	5.2	0.28	0.06	4.8	--	--
	--	0.21 (H)				
	--	0.255				
Pike	0.43	0.24	0.0485	4.4	--	--
	--	0.2 (H)				
	--	0.255				

TABLE 1 (Continued)

/15

Form	Average Mass, kg	Internal Radius (r), mm	r^2, mm^2	Radius of Curvature (R), mm	Volume of the Ampula (V), mm^3	$\frac{r^2R}{V}$
Spiny shark.....	1.15	0.26	0.0575	4.7	--	--
	--	0.22 (H)				
	--	0.25				
Skate.....	11.5	0.35	0.11	6.3	--	--
	--	0.31 (H)				
	--	0.335				
Tusk.....	13.5	0.26	0.065	4.8	--	--
	--	0.19 (H)				
	--	0.235				

Note: H is the horizontal canal; the mean value $\frac{r^2R}{V} = 0.0509 \pm 0.0264$.

The results of the measurements confirmed the theoretical predictions of the authors on the weak degree of dependency of r and R upon the body mass m: r^2 (or R) = Am^n, where A is the proportionality factor, and the size of the indicator degree is within the range from 1/12 to 1/3. Actually,

$$\log 100r^2 = (0.0945 \pm 0.0549) \quad \log + 0.2525,$$
$$\log 100R = (0.0761 \pm 0.0402) \quad \log + 2.3797,$$

where r and R are measured in millimeters; m in kilograms.

Thus, measurements indicated that r^2 and R have a tendency to increase very slowly with the animal's increase in mass, whereby the speed of increase for R is approximately the same as r^2; that is, significantly greater than r. The variations in r and R are small in comparison with the changes in size of the animals (Table 1), so that a 1000-fold growth in body mass among mammals, let us say, from 0.1 to 100 kg (assuming an equivalent 10-fold increase in the linear measurements of the body) corresponds to the increase in r by 1.6 and R by 2.2 times. The scattering of the mean values of r and R is substantially decreased if fish are excluded from the calculation; their canal sizes are significantly greater than the sizes of canals for mammals of the same mass.

The Otolith Apparatus

The receptor system for the measurement of linear acceleration with the aid of the motion of denser particles in a less dense fluid is universal for living organisms. /16

Both the statocyst apparatus of invertebrates and the otolith apparatus (utriculus, sacculus, lagena) of vertebrates function in this way.

The fluid inside the labyrinth of vertebrates (endolymph) has a density relative to water of 1.02-1.04. Large (from 1 to 20 mm) otoliths consist of limestone with a density of 2.93, having a mass consistency similar to toothpaste and to stones with a characteristic laminar structure. Otoconius in mammals and man (from 1 - 20 μ) consists of calcite with a density of 2.71. Certainly the protein network including the otoconius, the so-called otolith membrane, moves as a single body; i.e., its parts are very firmly interconnected. The density of the otolith formation, thus, is almost three times more dense than the endolymph, and the mass is as much as 100 times greater than the mass of an equal volume of endolymph. Consequently, the expression $\alpha V (\rho_1 - \rho_2)$, where α is acceleration, V volume, ρ_1 and ρ_2 the density of the otolith and endolymph, defines the surplus force which is applied to an otolith upon the action of gravitational or any other linear acceleration (Trinker, 1962).

The otolith membrane is penetrated with filiform processes (cilia) of the underlying layer of secondary sensory cells which, together with the intermediate supporting cells, form the sensory epithelium macula.

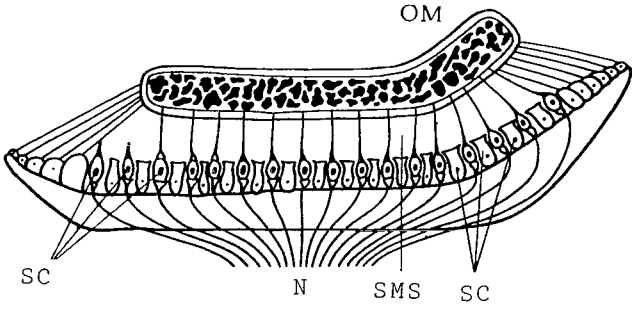

Fig. 3. Structural Scheme of the Otolith Organ (Longitudinal Section of the Otolith Membrane and Macula) (Groen, 1956).

OM - Otolith Membrane; SMS - Submembranal Space. Remaining Designations as on Fig. 2.

Between the otolith and macula there is a narrow space filled /17
with a jelly-like mass which makes it possible for the otolith to slide along the macula and to deform the hairs of the sensory cell. The maximum displacement of an otolith along the macula is on the order of 0.1 mm for the sacculus and 0.005 mm for the utriculus (de Vries, 1950) (Fig. 3).

Weighing the otolith of the sacculus, utriculus and lagena of bony fishes, de Vries, 1950, showed that the weight of otoliths changes insignificantly in comparison with the change of size (weight) of the fish (Table 2).

TABLE 2

WEIGHT OF OTOLITHS OF FISH (de Vries, 1956)

Form	Weight, g	Weight of Otoliths, mg		
		sacculus	utriculus	lagena
Pike	35	4,4	0,5	0,5
	3000	51,0	6,0	6,5
Ruff	6	7	0,16	—
	27	35	0,65	12

The general law of the significantly slower increase in sizes of the labyrinth in comparison with the increase in the size of the animal is true for all sections of the labyrinth. This is understandable since the labyrinth is "not the ship's helm, but only its compass" (de Vries, 1956). It is interesting that for mammals the membranous labyrinth does not grow after birth, although the temporal bone in which it is included increases significantly.

Brief Morphological Information on the Structure of the Sensory Epithelium of the Vestibular Apparatus

In the acoustical lateral system two types of receptor cells are differentiated: Type 1 and Type 2. Type 2 is characteristic for the organs of the lateral line, the vestibular portions of the internal ear of lower vertebrates and for Corti's organ of birds and mammals; Type 1 for the vestibular portion of higher vertebrates (reptiles, birds and mammals). In the sensory epithelium of the cristae and maculae of higher vertebrates, two types of receptor cells are known; pitcher-shaped Type 1 cells and cylindrical Type 2 cells (Wersall, 1956, Fig. 4). The basic difference between these two types of receptor cells consists in the distribution and structure of nerve endings, and in the distribution of cellular organells.

At the same time Type 2 cylindrical receptor cells are innervated by numerous thin nerve fibers, forming on their basis the bud-shaped nerve ending of the second type (granulated and non-granulated) Type 2 receptor cells are surrounded with large cup-shaped nerve endings almost to the very tip (Fig. 4). Engstrom (1958) discovered the presence of small granulated nerve endings, forming synapses of the exterior of this nerve cup. The nerve cup may give rise to processes which enter into synaptical contact with Type 1 cylindrical cells (Ades, Engstrom, 1965).

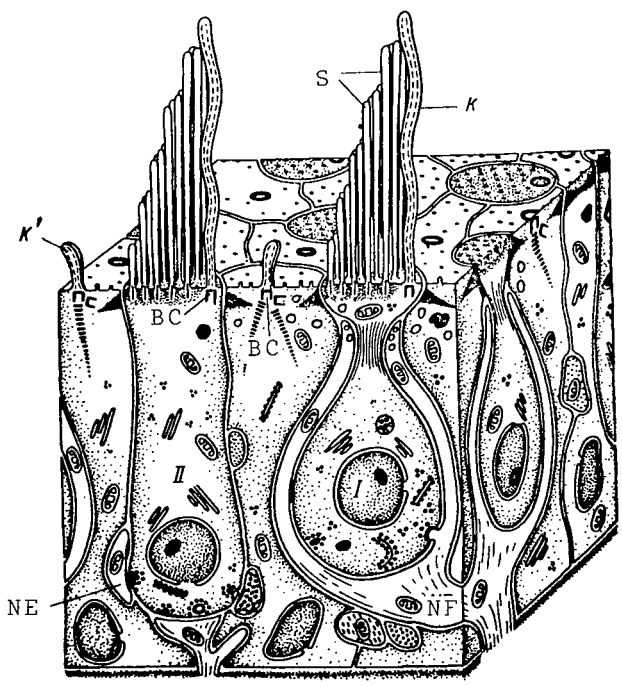

Fig. 4. Structural Scheme of the Vestibular Sensory Epithelium.

NF - Nerve Fiber, Forming a Calyx Around a Type 1 cell; NE - Nerve Ending for a Type 2 cell; S - Sterocilia; K - Kinocilia with a Basal Corpuscle (BC); K′ - Reduced Kinocilia (Spoendlin, 1965a).

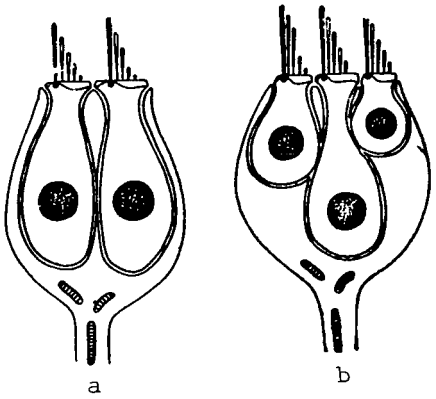

Fig. 5. Schematic Drawing of the Variety of Scyphoid Endings.

(a) Double and (b) Triple Cups (Spoendlin, 1956b)

Sometimes there are from 2-4 Type 1 cells in one cup (Fig. 5). /19
Unlike the bud-shaped nerve endings, the scyphoid nerve endings are formed with thick nerve fibers, each of which gives a small number of scyphoid endings to the neighboring receptor cells. Although both types of cells are distributed along the entire stretch of the ampullar cristae, Type 1 cells are localized chiefly under apexes, and Type 2 cells basically in the peripheral regions. In maculae Type 1 cells are often found mainly in the central regions, since on the periphery more of the cells are of Type 2. Evidently, there are more Type 2 cells in maculae than in cristae. These data and also those on the more differentiated distribution of organoids in the cytoplasms of Type 1 cells allowed Wersall (1956) to draw the conclusion that the cylindrical Type 2 receptor cells which are found in all vertebrates, receive a strong diffuse stimulus, while Type 1 receptor cells are highly differentiated cells with a specific function and receive local actions on a limited region of the sensory epithelium.

In a large number of investigations, Ya. A. Vinnikov and others (Vinnikov, 1966) in particular discovered cytochemical differences between Type 1 and Type 2 receptor cells in the utricular macula of many mammals and birds. These differences primarily concern the character of the distribution of RNA, protein, and functional groups of protein molecules.

Receptor hair cells of the cristae of the semicircular canals in vertebrates and of lateral line organs are characterized by the presence of one mobile kinocilium with a characteristic (18 + 2) fibrillar structure. It is orientated beside a hair bundle with little mobility which has lost fibrils, the so-called sterocilia (Fig. 6a).

The kinocilium is located in a notch formed by 8 or 9 parallel rows of sterocilia (5-6 per row). Sterocilia bundles have various lengths. The longest sterocilia are distributed around kinocilium and attain longths of 40 μ (Wersall, 1956). To date no differences have been discovered in the structure of sterocilia in hair bundles of the Type 1 and Type 2 sensory cells.

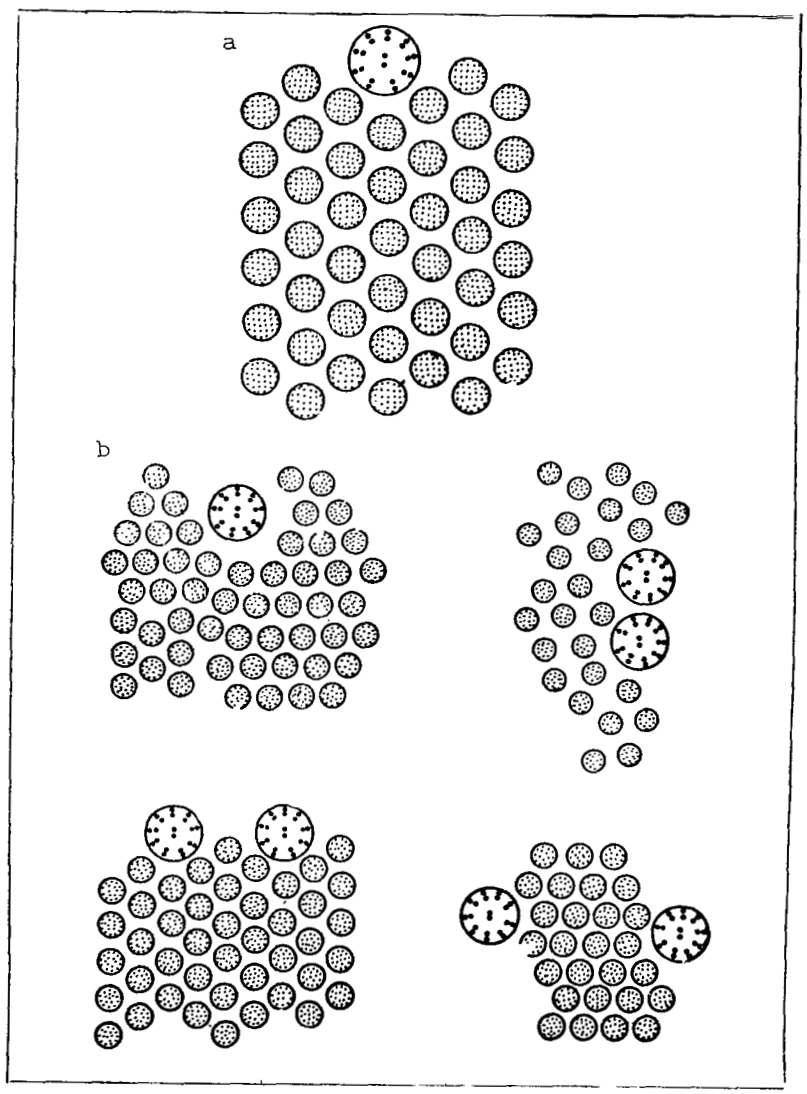

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Fig. 6. Various Types of Hair Bundles: (a) Cristae and (b) Maculae (Ormerod, 1965).

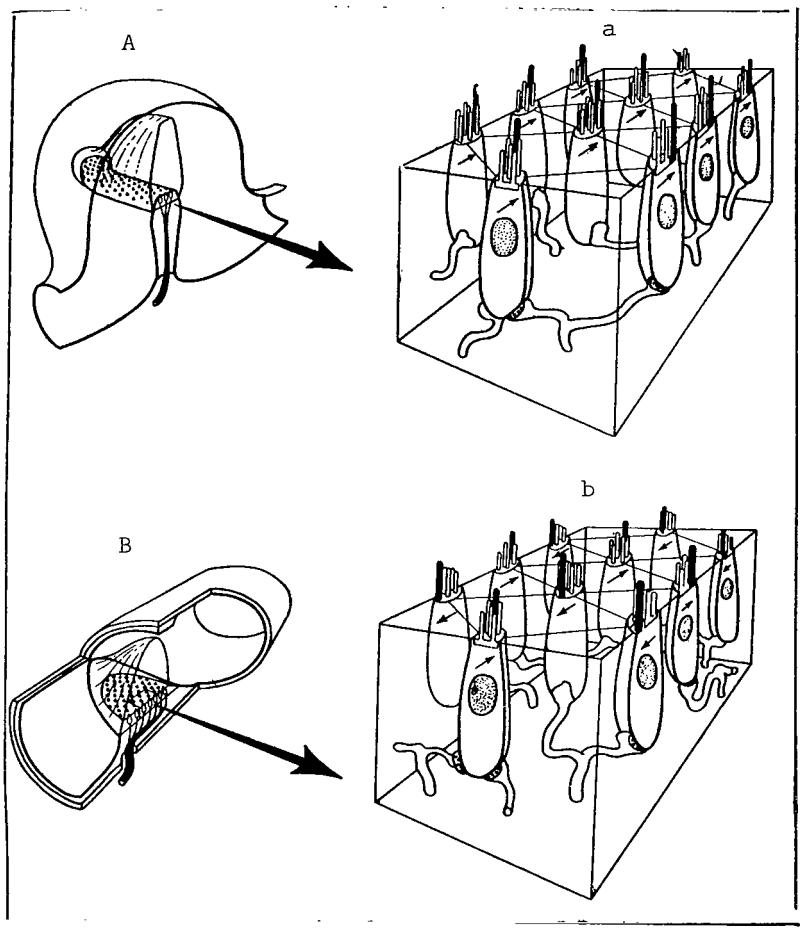

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Fig. 7. Microscopic Structure of the Crest of the Ampulla (A) and the Lateral Line Organ (B).

(a) and (b) Magnified Portions of the Sensory Epithelium, Illustrating the Structure of the Sensory Cells and the Orientation of Hair Bundles. Black Kinocilium (Flock, Wersall, 1962).

In the macula utriculus, in addition to the described type of organization of hairs into a bundle, other types appear (Fig. 6b). /22

In the crista of the horizontal semicircular canal, the kinocilium in all hair bundles is found at the side of the utriculus; in the crista of the forward verticular canal it is located on the side facing the open space of the canal (Wersall, 1956; Lowenstein, Wersall, 1959) (Fig. 4).

Such a homogeneous polarization, as the investigations of Flock (1964) showed on the burbot, Lowenstein et al., (1964) on the skate and Spoendlin (1956) on monkeys, does not exist in other regions of the vestibular apparatus.

In macula utriculus the directions of polarization are distributed in a fan-shape from the medial portion of the macula to several distorted border lines, from which the polarization of the sensory cells is the opposite (Fig. 8). Thus, in the macula utriculus all possible directions of polarization are presented.

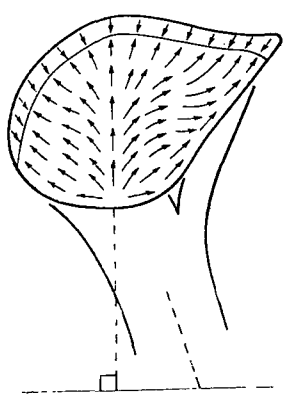

Fig. 8. Schematic Drawing of the Morphological Polarization of Hair Cells in the Macula Utriculus of the Burbot (Lota vulgaris) (Flock, 1964).

In the macula sacculus the cells are polarized approximately equally in the front lower and rear upper directions whereby the kinocilia in both directions of the border line are turned in opposite sides, so that in the macula sacculus not all directions of polarization are represented.

Polarization of various sections of the vestibular apparatus of the skate (Raja clavata) is presented in Figure 9.

There are 6,900 sensory cells in the macula sacculus of the guinea pig; 8,400 in the macula utriculus; 6,000 in the crista of the horizontal semicircular canals; and the surface area of the sensory epithelium approximately 0.48, 0.55 and 0.40 mm^2 (Lindeman, 1967).

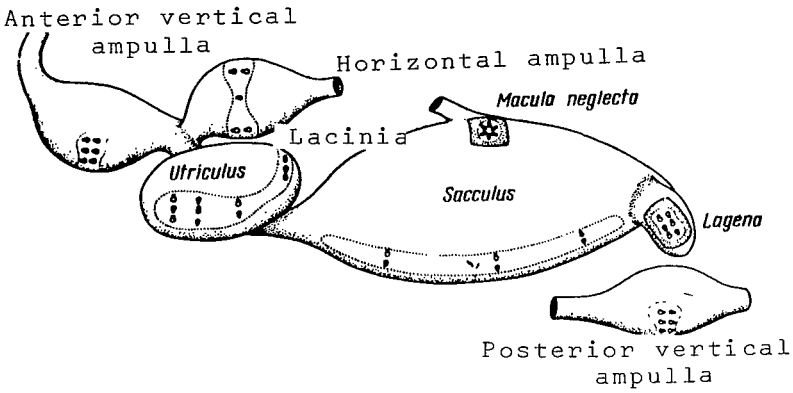

Fig. 9. Morphological Polarization of the Sensory Epithelium in Various Sections of the Labyrinth of the Skate Raja clavata (Lowenstein et al., 1964). /23

Between the hair cells of the sensory epithelium there are support cells shaped like irregular prisms. Support cells densely encircle the sensory cells and nerve endings. Several of them stretch from the basalar membrane to the epithelial surface, whereas others do not reach the base of the sensory cells.

Below the sensory epithelium is located a thick network of capillaries. In the direction toward the basalar membrane, the walls of the capillaries become thin and are punctured with pores on the order of 800 Å in diameter (Flock, 1965).

Chemical Composition and Biophysics of the Labyrinth Fluids

Recent investigations by Maggio (1966) on disturbances in the cochlear function of cats, caused by partial removal of perilymph through the round window, as well as his demonstration of dynamic connections between several basic chemical, electrophysiological and morphological indicators of activity in the auditory system in cats and Dalmation dogs with congenital deafness, led the authors to the following conclusion. The perilymph and probably the endolymph are not only media enabling the transmission of mechanical energy of sound to the hair cells, but they probably are primarily electrochemical and physical chemical media, necessary for the existence of the functions of the labyrinth's neuroreceptors. Therefore, for example, as a consequence of the partial removal of the perilymph from the cochlea not only the conditions of energy /24

transmission to the hair cells, but also the very processes of conversion of mechanical sound energy into electrical energy of the nerve impulses are hindered. The authors extend their conclusions even to the receptors of the vestibular apparatus. It is absolutely necessary that there be further experiments to test the proposed hypotheses.

Given briefly below are summary literary data related to the biochemical composition of labyrinth fluids in comparison with the cerebro-spinal fluid and with blood serum. It is necessary to note that the majority of data were obtained after death and, according to Maggio (1966), the K^+ and Na^+ content cannot be considered absolutely reliable.

Comparison of Physical Characteristics and Physical Composition of the Perilymph and Endolymph

The viscosity, specific gravity, osmotic pressure, electrical conductivity and biopotentials of the perilymph are lower than those of the endolymph. The volume, pressure diffraction and indicator and electrical conductivity is higher in the perilymph. Just on the basis of these facts it is possible to come to the conclusion that the endolymph and perilymph are different fluids. Just what role is played by the physical characteristics of these two fluids has not yet been established, and there are only suppositions. For example, the dependency between the viscosity of the perilymph and the mechanism of energy transformation in the cochlear and vestibular systems is not known. The high viscosity of the endolymph (with a maximum in elasmobranch fish) is due to a high content of mucopolysaccharides. As a result of such a viscosity the effects of strong oscillation of the endolymph may be eliminated, and the vortical motions with the physiological current of this fluid may be prevented (Tonndorf, van Bergeijk, 1958). The different composition of mucopolysaccharides in elasmobranch fish and in mammals determines the different viscosity of the endolymph of these vertebrates. In sharks, however, the viscosity of the perilymph is higher than the viscosity of the endolymph. The perilymph of the utriculus and of the semi-circular canals is more viscous than the perilymph of the cochlea and the sacculus. Basically, mucosaccharides in the labyrinth fluid of sharks are represented by hyaluronic acid. It appears important that cochlea and vestibular structures such as the tectorial membrane, the cochlear and the otolith membrane are not only washed but also saturated with endolymph containing mucopolysaccharides.

The high osmotic pressure in the endolymph relative to the perilymph supports the point of view that the endolymph is a product of an active process of secretion of the stria vascularis cells, and the perilymph can be used as an ultrafiltrate of serum through the capillary (we will deal with this below). /25

The high indicators of refraction of the perilymph relative to the endolymph, despite the greater viscosity of the latter, can be ascribed to the larger protein content in the perilymph connected with inorganic ions (Na^+, Ka^+, Ca^{++} etc.).

The content of organic substances in the perilymph is higher than in the endolymph, and the content of inorganic substances is lower. In the cat, the concentration of proteins in the perilymph is twice, in the guinea pig three times and in a shark one and one-half times higher than in the endolymph. The general nitrogen, however, is slightly higher in the perilymph of sharks. In the guinea pig, the amount of nonprotein nitrogen is the same in the perilymph and the endolymph. In mammals the picture of the protein fraction in the perilymph differs from that in the endolymph. Approximately one and one-half of the proteins of the perilymph are albumins. In human serum, on the other hand, albumins comprise 4/5 of all proteins. In other body fluids (vitreous body) the albumin concentration is equal to the concentration of globulins. In the lower vertebrates, such as elasmobranch fish, the proteins of the endolymph are represented only by globulins, whereas in the perilymph by globulins (79%) and albumins (21%).

Amino acids of the perilymph belong to the aliphatic mono- and diamino acids with low molecular weight. They also belong to the class of glycoform acids and consequently participate in various phases of glucose metabolism. The composition of amino acids in the perilymph does not change with intra-abdominal introduction of triptophan (absent in the perilymph) and glocu-amino acid which, on the other hand, is present in it (Chevance et al., 1960); but it does change with the introduction of solutions containing alanine, serine, threonine and methionine. A difference of the perilymph is the presence of glutoamino acid in the absence of methionine. It is possible to assume that the constancy in the composition of amino acids is due to a local enzymatic balance. A complex barrier controlled by the vegetative nervous system excludes metal ions and several free amino acids from the labyrinth fluid, and especially from the perilymph (Chevance, 1958, Chevance et al., 1960; Kluyskers, Rabacy, 1960).

In the shark and the cat the pH of the perilymph and the endolymph are approximately equal (Vilstrup, Jensen, 1955; Ledoux, 1950), but in the guinea pig the pH of the perilymph is higher than in the endolymph, in which the insufficiency of O_2 lowers the pH to 7.8 and 7.0, respectively (Misrahy et al., 1958). In man the pH in the endolymph is higher than in the perilymph (Rauch, Kostlin, 1958).

The concentrations of Ca^{++}, Mg^{++}, Cl^- in the perilymph and endolymph of mammals are equal, but that of Na^+ is greater in the perilymph and K^+ in the endolymph. The concentration of Na^+ in the /26

perilymph is closely connected with the concentration of the K^+ in the endolymph. In elasmobranch fish the ratio of the concentrations of endolymph and perilymph for K^+ is 19 (compared with the ratio in mammals), for Na^+ is 1.05, for Cl^- is 1.2, and in mammals this ratio for Na^+ is 0.1 and for Cl^- is 0.9 (Murray, Pottz, 1961). The total concentration of Na^+ and K^+ is greater in the endolymph. The high concentration of Cl^- balances the high concentrations of Na^+ and K^+. The labyrinth fluid of the octopus (Octopus vulgaris) is similar in ion composition to blood serum (Amore et al., 1959).

On the whole the given data indicate that the endolymph and the perilymph are different fluids in their physical characteristics and in their chemical composition, and apparently have different origins.

Comparison of the Physiological Characteristics and Chemical Composition of the Perilymph and Endolymph

The osmotic pressure, freezing point and the indicator of refraction of the perilymph is higher than that of the cerebrospinal fluid, and its electroconductivity is lower.

Organic substances (proteins, ureas, amino and ketoacids, etc.) in the perilymph are greater than in the cerebro spinal fluid. There are more of the substances in the perilymph as opposed to the cerebro-spinal fluid by 5 times in the cat and by 3 times in the guinea pig and man. The content of inorganic substances is the same, with the exception of CO_2, the concentration of which is higher in the cerebro-spinal fluid (in man). In mammals there is also a difference in the concentrations of amino acids.

Finally, the activity of phosphomonoesterases and lactatedehydrogenases is higher in the perilymph. These data indicate that these fluids are similar but are not identical. The hypothesis that perilymph is a dialyzate of the cerebro-spinal fluid cannot be considered to be correct. It is more similar to blood serum than to endolymph.

The osmotic pressure and the indicator of refraction of the endolymph is higher than that of the cerebro-spinal fluid.

The concentration of H^+ in the endolymph is higher and the content of reducing substances is lower. The content of proteins and the concentration of Ca^{++} and Mg^{++} are approximately equal. In the cat and several elasmobranches such as Raja clavata, Cetorhinus maximus and Scoloidontus laticandus, the content of Cl^- in the endolymph is higher. In bony fishes the low concentration of Na^+ and in the elasmobranch fish the high concentration of Cl^- in the endolymph partially compensates for the excesses

of K^+ (Enger, 1964).

Comparison of the Physical Characteristics and the Chemical Composition of the Perilymph and the Endolymph in Blood Serum

The osmotic pressure and the indicator of refraction of these /27
fluids are approximately the same.

There are less organic substances in the perilymph than in blood serum. The concentrations of Na^+, K^+ and Ca^{++} are the same. The picture of the fractions of proteins, amino and ketoacids is approximately the same in both fluids. Glycine and taurine, however, predominate in the perilymph; the activity of phosphomonoesterase and lactate dihydrogenase is higher. In human perilymph, inorganic substances (Na^+) are greater, and CO_2 and inorganic phosphorous are lower. The quantities of K^+ and Mg^{++} are approximately equal.

From physical and chemical points of view these fluids are very similar; therefore it is permissible to view the perilymph as an ultrafiltrate of blood serum.

The osmotic pressure and the refraction indicator of the endolymph is lower than that of blood cells.

In the endolymph the content of proteins and urea is higher, and phosphomonoesterase and lactate dihydrogenase are less active. In the cat, the concentrations of K^+ and CO_2 are higher in the endolymph, and in man, on the contrary, the concentrations of K^+ and CO_2 are higher in blood serum. The amount of inorganic phosphorous is the same.

These data indicate that it is impossible to view the endolymph as an ultrafiltrate of the blood, but it must be considered the result of a secretion process of the stria vascularis cells, insuring the retention of Na^+ and the liberation of K^+, mechanisms similar to the processes in the renal caniculi.

If blood serum by its Na^+ and K^+ content is close to extracellular fluid, then endolymph is close to intracellular fluid. Endolymph is the only body fluid in which the concentration of K^+ is the same as in the introcellular fluid. In the extracellular fluid K^+ = 18-22 mg per 100 ml; in human saliva 77.0 (46.4-107.6) mg/100 ml (White et al., 1955).

In 1951, Békésy registered an unusually high positive potential (+ 70-80 mV) in the endolymph of the cochlea in the guinea pig in relationship to that of the perilymph. Further investigations (Smith et al., 1958; Eldredge et al 1961) showed that despite the anatomical continuity of the labyrinth fluids, the potential

of endolymph in the sacculus of the guinea pig is a total of +1 mV; in the utriculus +4 mV; in the ampulla of the semicircular canal -1 mV. Consequently the electric polarization of the scala media of the cochlea is not connected with the concentration gradient of K^+ and Na^+ in the endolymph and perilymph. A number of authors (Davis et al., 1958; Tasaki, Spyropoulos, 1959) indicated convincingly that the source of the endocochlear potential is the stria vascularis.

The significance of the high concentration of K^+ in the endo- /28
lymph and the existence of a rest potential of +70-80 mV in the endolymph of the cochlea of mammals is not understood at the present time. Tasaki (1960) proposed that the endocochlear potential has an action on the receptor cells similar to the action of an anode on excitable tissue, immersed in a solution rich in K^+ ions. Under these conditions the positive polarization not only restores the irritability of the cellular membrane, saturated in the solution of K^+ ions, but even makes the membrane extremely unstable, capable of producing sharp oscillations of the membrane potential, particularly in response to mechanical action. Similarly, the hair cells are polarized by the endocochlear potential to a critical level; i.e. they are at a level near to a spontaneous change in the potential (due to thermal noise). Under the conditions the slightest mechanical action can give impetus to a large change in potential, which leads to the appearance of a nerve impulse. Thus the existence of the endocochlear potential (and conditions of high concentration of K^+ ions in the endolymph) insures (apparently) a high sensitivity of the mechanism of mechanical energy transformation in the process of hair cell excitation. From this point of view, the existence of a negligible potential in the endolymph of the vestibular apparatus might signify that its mechanism had a lower sensitivity than that of the cochlear mechanism, at least in relation to the role played by the potential of the endolymph in the process of the transformation of mechanical energy to electrical energy.

It is necessary to note that during the process of evolution, the value of labyrinth potential grows (Schmidt, Fernandez, 1962).

The Physiology of Vestibular Receptors

Microphone Effect

In 1930, Wever and Bray, listening on a loudspeaker to the potentials of the cochlear nerves of a cat with sound stimulation of the ear, discovered that the outgoing potentials reproduced the shape of an incident sound wave so well that it was not only possible to hear distinctly each word which was pronounced by the experimenter, but it was also possible to distinguish by voice people speaking simultaneously. It appeared that the auditory nerve acts

like a telephone cable. But in 1931 Adrian showed that the electrical changes which are registered are generated by the cochlea itself and are not due to nerve impulses. "The cause of the effect", wrote Adrian, "appears to be a kind of microphone action, by means of which acoustic oscillations produce changes in potential between the various points of the inner ear." The systematic study of the /29
phenomenon by many investigators leaves no doubt about the fact that the microphone response (effect, action) of the cochlea expresses the activity of the receptor (not nerve) elements of a peripheral section of the nervous system (Davis, 1957). One characteristic of the microphone effect is complete reproduction of the shape of the actuating sound wave in the pattern of electrical potentials (currents) which are registered by placing electrodes at any point which is electrically connected with the fluid medium of the passages of the cochlea of the inner ear (Gershuni, 1964). What is the functional significance of this phenomena?

The significance of the microphone effect in the cochlear process of transformation of mechanical changes to a nerve impulse is insufficiently clear. At the present time, the most widely held concept is that the microphone response is an electrical expression of processes forming a necessary intermediate link between mechanical and nerve processes in the cochlea (Davis, 1957; Gershuni, 1964). Therefore the investigation of the characteristics of the microphone response is one of the effective means of studying the activity of receptors.

The microphone response of the cochlea was observed in all vertebrate animals investigated to date: in man, monkeys, dogs, guinea pigs, cats, rabbits, hamsters, mice, opossums, alligators, turtles, pigeons, skates and frogs. It resulted that the microphone effect is not limited to the cochlea. It appears in all labyrinth receptors (Pumphrey, 1939; Zotterman, 1943; de Vries, Bleeker, 1949; Trincker, Partsch, 1959). In 1948 the microphone response was discovered in the lateral line organ of fish (de Vries, 1948), which is morphologically homologous to the vestibular apparatus (Pumphrey, 1950; Lowenstein, 1960; Granit, 1957; Flock, 1965). The common origin of these organs is reflected not only in the similarity of structure, but probably in the similar principles of receptor mechanisms. Because of its accessibility and relative simple organization, the lateral line organ of fish became a convenient model for the investigation of the basic characteristics of microphone activity of all acoustico-lateral systems (Jielof et al., 1952; Kuiper, 1956; Harris, Bergeijk, 1962; Flock, 1965, et al.).

The frequency of the microphone potential in the lateral line organs of fish, as opposed to that of the cochlea (Tasaki et al., 1954) and of the ampullar cristae (de Vries, Bleeker, 1949), is equal to twice the frequency of the stimulus (Fig. 10). Microphone

frequencies which differed from the frequency of stimulation were observed in otolith organs (Zotterman, 1943; de Vries, 1956). Insofar as the impulse displacement of the cupula in either of the two opposite directions causes a negative potential; the microphone response consists only of negative peaks, i.e. a negative peak corresponds to each deflection of the oscillating cupula.

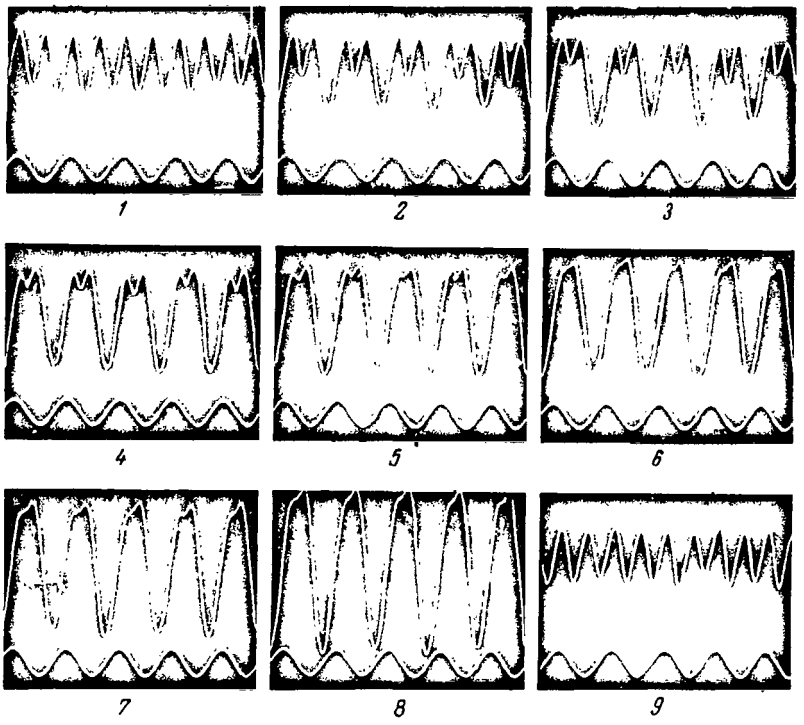

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Fig. 10. Influence of Static Displacement of the Cupula on the Microphone Potential. To a Cupula Which Oscillates with a Constant Amplitude There is Imparted a Rostral Displacement at a 5 μ Interval. 1,2,3,4,5,6, 7,8,9 - Respectively 0, 5, 10, 15, 20, 25, 30, 35 μV. The Scale of Time is 0.5 msec, the Amplitude of Oscillations 10 μ, Calibration 20 mV (Flock, 1965).

With purely sinusoidal oscillations of the cupula, the microphone response has a symmetrical sinusoidal shape. If a static displacement is imparted to the cupula, then the waveforms of the microphone potential gradually change, and when the displacement exceeds the amplitude of oscillations, the frequency of the microphone response is transformed into the frequency of the stimulus, but the waveform will differ from a truly sinusoidal one by the depression of the crests which are directed upwards (Fig. 10).

If now the cupula returns to its original position, the microphone response will again acquire a normal form. The greater the amplitude of oscillation,the greater the shift required of the cupula in order to make the transition from a double frequency of microphone potential to a single one (Flock 1965). Figure 10 shows that with a displacement of 20 μ, the amplitude of microphone potential is increased by 2 and with displacement of 35 μ, by 3 times in comparison with the original value. With a static displacement of /31
the cupula, directed to the head of the fish, a negative crest will grow, corresponding to the deflection of the cupula of the same direction in an oscillating motion, since with a displacement of the cupula in the direction towards the tail, a phase shift of 180° is observed, so that the crest grows corresponding to the caudal deflection of the cupula.

With both an oscillating and an impulse stimulation of the cupula, the microphone potential reflects the amplitude and not the speed of stimulus (Jielof et al., 1952; Kuiper, 1956; Harris, Bergeijk, 1962; Flock, 1965). This same result was obtained by Békésy (1951a) on the cochlea. As Holst (1950) and Trincker (1962) showed, even in the otolith organ displacement appears to be an effective stimulus.

The amplitude of microphone response with an increase in amplitude of oscillation changes according to nonlinear law. It grows swiftly with small amplitudes of oscillation, slower with larger ones and finally attains its extreme value ("saturation"). This dependency, constructed in double logarithmic coordinates, represents a linear function in a definite band of amplitudes of stimulation (from 3 - 5 μ) (Harris, van Bergeijk, 1962; Flock, 1965), which is also true for the microphone response of the cochlea (Wever, Lawrence, 1954; Davis, Eldredge, 1959).

The maximum amplitude of microphone response is usually from 100 - 200 μV with an amplitude of oscillation on the order of 10 μ (Jielof et al, 1952; Kuiper, 1956; Flock, 1965). The minimum amplitude of oscillation sufficient to produce a registered microphone response is usually on the order of 0.1 μ.

With all other conditions being equal, the amplitude of microphone response is greatest when the direction of oscillation is parallel to the axis of the lateral line canals. With a gradual deviation from this direction the amplitude diminishes, and it reaches its minimum value when the direction of stimulation is perpendicular to the axis of the canal (Fig. 11).

As was shown by the investigations of Kuiper (1956) and Flock (1965), the microphone response of the lateral line organ is always accompanied by a slow change in the negative potential.

The general theory proposed for the function of the hair cells in the acoustical lateral system maintains that a displacement of the sensory hairs in the direction from the sterocilia to the kinocilia, or in the cochlea in the direction of the centriole[1] is excitory and causes depolarization and an increase in the impulsation frequency innervating nerve fibers, since a displacement in the opposite direction leads to hyperpolarization and a decrease in the frequency of afferent discharge (Lowenstein, Wersall, 1959; Flock, Wersall, 1962; Flock at al., 1962; Engstrom et al., 1962; Dijkgraaf, 1963; Gorner, 1963; Lowenstein et al., 1964; Flock, 1964; Wersall, Flock, 1965; Flock, 1965).

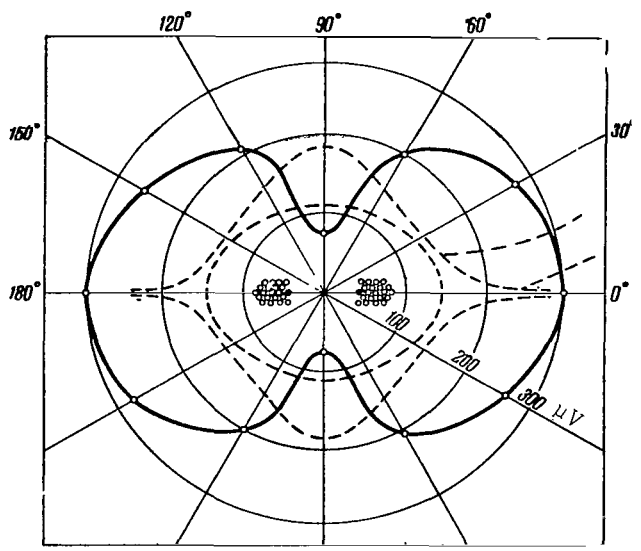

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Fig. 11. Diagram of Directed Sensitivity of the Lateral Line Organ in a System of Polar Coordinates, the Microphone Potential with Each Direction of Stimulation is Plotted on the Corresponding Coordinates. The Axis of the Canal is Parallel to the Coordinate 0° - 180°. The Outline of the Organ is Indicated by the Dotted Lines. In Hair Bundles, Black Kinociliam (Amplitude Oscillations, 4 μ, Frequency 100 Hz) (Flock 1965).

[1]The centriole corresponds to the basilar corpuscle of the kinocilia of the hair cells in the vestibular apparatus and the lateral line organ, and correspondingly the correlation between the functional and morphological polarization for external hair cells is the same as for hair cells in the vestibular apparatus and the lateral line organs.

Consequently, the frequency of microphone potential generated by the hair cell must be equal to the frequency of the stimulus. In the cochlea and in the ampullar cristae the hair cells are oriented in one direction, and the frequency of microphone response is equal to the frequency of the stimulus (Tasaki et al, 1954). In the cochlea, the centrioles of the external hair cells are oriented in a radial direction opposite Corti's tunnel (Flock et al., 1962; Engstrom et al., 1962). Békésy (1953) showed that displacement of the vibrating needle in the direction of the spindle leads to depolarization, and the opposite displacement elicits hyperpolarization. In the ampullar crista of the horizontal semicircular canal a displacement of the cupula in the direction of the utriculus appears to be excitory (Lowenstein, Sand, 1940; Trincker, 1957) and corresponds to a direction of displacement toward the kinocilia (Lowenstein, Wersall, 1959).

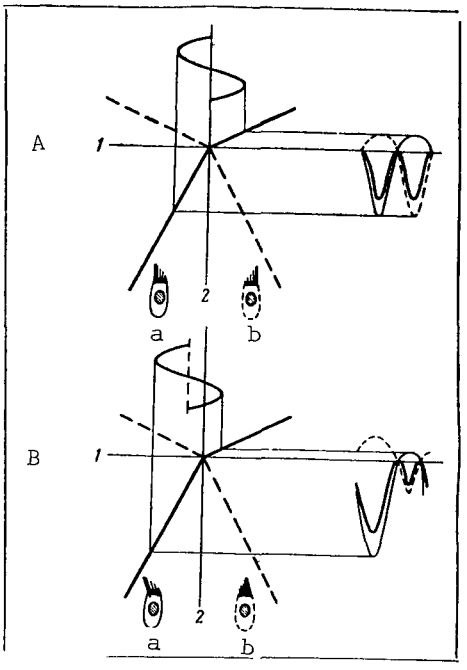

Fig. 12. Schematic Drawing Illustrating the Theory of the Generation of Microphone Potential in the Lateral Line Organ (Flock, 1965). /33

(A) Theoretical Form of a Microphone Potential with Oscillation of the Cupula Around a Neutral Position; (B) The Same with Oscillation of the Cupula Displaced Relatively Neutral to the Left.

(a) and (b) Oppositely Orientated Hair Cells; (1) Amplitude of Displacement of the Cupula from a Relatively Neutral Position; (2) Amplitude of Microphone Potential.

The microphone response of the lateral line organ has a frequency equal to double the frequency of the stimulus (Jielof et al, 1952; Kuiper, 1956; Flock, 1965). But in this organ there are two groups of hair cells which are oriented in opposite directions. Consequently, the registered microphone potential is the sum of potential generated by two groups of cells and the double frequency is explained, correspondingly, by the superposition of two opposite responses (Flock, Wersall, 1962). The inequality of simultaneously generated potentials is a necessary condition of the fact that

nevertheless it is possible to register the microphone response, since in the opposite case they would extinguish one another. The fact that depolarization is greater than hyperpolarization follows from the fact that impulse displacement of the cupula in any direction always causes a negative shift of potential (Flock 1965). Consequently the theory must assume, at least for the lateral line organs, nonlinearity of receptor functions.

The explanation given by Flock (1965) for the generation of normal symmetrical microphone response is presented in Figure 12A. In this figure, in a Cartesian system of coordinates, transmission /34 "input-output" functions of two hair cells, oriented in opposite directions, are constructed. The abscissa represents the displacement of the cupula or of sensory hairs, and the ordinate indicates the negative or positive receptor potential, i.e. depolarization and hyperpolarization respectively.

"Input" is the oscillatory shift of the cupula with vibrational stimulation presented in the form of a sinusoidal wave from the same abscissa, but time is plotted along the ordinates. The "output" is represented on the right; the microphone potential is on the ordinate; time on the abscissa.

During the first half of the period of stimulation the cupula is displaced, relative to the cell, in the excitory direction, and cell a responds with a gradual deformation, which at each moment is proportional to the shift of the cupula. Simultaneously the elicited response of cell b is hyperpolarization since it is stimulated in the direction from the kinocilia to the sterocilia. During the second half of the period cell b is excited and the activity of cell a is suppressed. Insofar as depolarization is always higher than hyperpolarization, the microphone output during each half of the period consists of one negative crest and has a frequency equal to twice the frequency of the stimulus (see Fig. 10). In every moment consequently, the registered microphone potential represents the result of the summation of depolarization and hyperpolarization. This conclusion has a serious relation to the question of energetic balance on the lateral line organ. If electrical energy emitted by the organ exceeds the mechanical energy of the stimulus, the generation of a microphone potential appears as a process demanding the application of energy from sources other than the stimuli and, most probably, from sources distributed in the hair cells themselves and therefore appears as a truly biological sensory effect. If this is not so, then the microphone potential may simply be a physiological effect, such as the piezoelectric effect or a physical displacement of molecular chains. Békésy (1951b) showed that the energy of the cochlear microphone response is greater than the energy of the stimulating cells. However, in similar measurements on the lateral line organ, Jielof et al. (1952) found that the energy of the recorded output is equal approximately to the energy of the stimulus. Subsequently de Vries (1956) indicated possible

errors in the calculation. It follows from the concept of Flock presented here that changes in potential which take place in the sensory epithelium of the lateral line organ are in fact greater than those which are registered. Thus, in this organ the energy of potential change, represented by the microphone output, is greater than the mechanical energy of the stimulus (Flock, 1965).

In Figure 12B the theoretical effect of static displacement of the cupula on the microphone potential is schematically diagrammed. The cupula is shifted by half the amplitude of stimulation to the left, which corresponds to a rostral displacement on the preparation, and it oscillates relative to this position. The displacement imparted to the cupula is transmitted by the sensory /35 cells. It is represented in Figure 12B by the deflection of sensory hairs. When stimulation begins, hair cell a is already in a depolarized operative condition. During the first half of the period, depolarization increases in proportion to the given displacement. During the second half of the period, the amount of depolarization diminishes up to the time when the cupula passes the equilibrium position. Further displacement to the right causes hyperpolarization. For hair cell b the imparted static displacement appears as hyperpolarizing, in that it displaces the sensory hairs in the direction from the kinocilia to the sterocilia. During the first half of the period, this cell functions in a condition of elevated hyperpolarization, and it produces depolarization only during that part of the second half of the period when the cupula has passed the neutral position. The registered microphone output appears as the sum of responses and is characterized by an increase in the negative crest, corresponding to rostral oscillation, which precisely corresponds to the microphone response, registered with experimental displacement of the cupula in a rostral direction. If the cupula oscillates with static displacement to the right of the neutral position, a shift of 180° appears which is observed even experimentally. Similar action of static displacement and microphone potential was noted also by other investigators (Jielof et al., 1952; Kuiper, 1956; Harris, van Bergeijk, 1962), but it was given another explanation. Zant (1937) discovered that static displacement which inhibited the afferent discharge suppressed the response to vibration in innervating nerve fibers. Evidently this dependency between displacement of the cupula and the character of microphone response is reflected by the frequency of impulsation in nerve fibers.

Figure 12B shows that with an increase in static displacement of the cupula, the amplitude of the negative crest will increase and, when the displacement becomes equal to the amplitude of vibration, the second harmonic disappears. With an increase in the amplitude of oscillation the displacement increases, which is necessary in order to analyze the second harmonic, as confirmed by the experiments of Flock (165) and earlier noted by Jielof at al. (1952) and Kuiper (1956). However in experiments the transition

period from the double frequency of microphone response to a single frequency takes place with a displacement greater than the amplitude of oscillation. This can be explained only by the phase-tonic reaction of the receptor, caused by the partial slipping of the cupula due to its plasticity, or by the adaptation of the sensory cells. This conclusion is based on the experimental fact that the /36 effect of static displacement is greater when the displacement begins, after which it weakens somewhat.

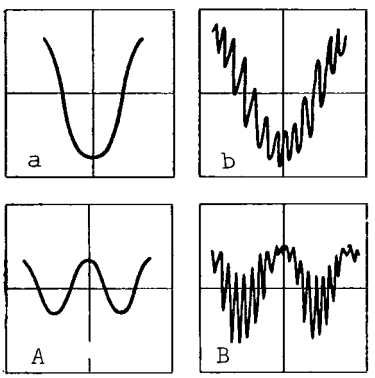

Fig. 13. The Effect of Superposition of Low and High Frequency Vibration on the Microphone Response.

(a) Low Frequency Vibration,
(b) Superposition of High and Low Frequency Vibration;
(A) Microphone Response to Low Frequency Vibration;
(B) The Same on a Superposition of Low and High Frequency Vibration (de Vries et al.,1955).

The intensification produced by static displacement of the cupula corresponds to the effect of superposition described by de Vries et al. (1955) and Kuiper (1956). If instead of a static displacement a low frequency vibration is superimposed on high frequency vibration, then a stress of high frequency microphone response in the negative phases of low frequency response is observed (Fig. 13). Consequently, the effect of superposition indicates nonlinearity of the transmission function of the sensory cells.

In Figure 12 the nonlinearity of the "stimulus-response" curve is presented on a linear scale with a sharp change in slope of the curves, on which the values of depolarization and hyperpolarization are plotted for various amplitudes of displacement in opposite direction. Such a very approximate idea of nonlinearity was applied by Flock for simplicity's sake. The microphone output with such a transmission function would have the shape of a distorted sinusoidal wave with the oscillation of the cupula around the position of equilibrium and would precisely reproduce a sinusoidal waveform of the stimulus if stimulation took place with a static displacement of the cupula which was equal to or greater than the amplitude of stimulation. However, as was shown in Figure 10 this does not take place.

Insofar as it is known that biological phenomena are often subject to exponential laws, Flock examines the possibility that the emission function of the hair cell is also exponential. In this case the graphically constructed waveform of the microphone

response precisely corresponded to that observed in the experiment. Intracellular registration of cellular activity must show whether the emission function of the hair cell actually is exponential. There are data, although still incomplete, indicating the nonlinearity of the sensory response in other organs of the acousticolateral system. Thus in the ampullar cristae Trincker (1957) discovered that the degree of depolarization attains a higher value than that of hyperpolarization, due to the displacement of the cupulas in the opposite direction. The well-known Ewald's law (1892) asserts that in the horizontal canal an excitory response to rotational stimulation must be greater than the inhibitory response elicited simultaneously in the opposite canal. Moreover, de Vries at al. (1955) demonstrated the effect of the superposition of microphone potential on the ampullar cristae of the pigeon. Consequently, even in this organ the sensory response is subject to a nonlinear function. /37

As was indicated above, the general theory of hair cell function asserts that displacement of sensory hairs in the direction from the sterocilia to the kinocilia appears as excitory and is accompanied by depolarization, i.e. by negative potential of the endolymph and an increase in the discharge frequency of the innervating nerve fibers. A displacement in the opposite direction causes hyperpolarization and inhibits afferent discharge. Thus, the hair cells are directionally sensitive and signal the direction of stimulation of bilateral modulation of sensory response. Hence Flock (1965) comes to the conclusion that displacement in a direction perpendicular to the orientation of the cells cannot be an effective stimulus.

As is shown in Figure 11, directional sensitivity of the organs approximately corresponds to the cosines of the output, generated during stimulation along the axis of the canal. It would be so in the case where a stimulus which generates a microphone potential would appear as a displacement vector component corresponding to the axis of canal. A purely cosinusoidal function would give two circumferences tangent at the beginning of the coordinates. On the same diagram, with a declination of the stimulating direction from the axis of the canal, the response is greater than the given cosine function, and correspondingly the response is not zero when the direction of stimulation is perpendicular to the axis of the canal. But from an electromicroscopic investigation (Flock, 1965) it is known that although the hair cells are basically oriented parallel to the axis of the canal, there are occasionally deviations by 10-15° from the main orientation. For these cells, displacement which is perpendicular to the direction of primary orientation will still have the displacement vector component, which is an effective stimulus, if the directional sensitivity of a single hair cell is defined by a cosinusoidal function. In this case the difference between the recorded and the theoretical

characteristics of the directional sensitivity of the organ may be explained by the overlapping responses of a single hair cell.

Direction of stimulation in innervating nerve fibers is signalled in both the lateral line organ (Sand, 1937) and the epidermal organ (Gorner, 1962) by bilateral modulation of the spontaneous discharge frequency. Displacement in one direction is excitory, /38
displacement in the other direction is inhibitory. There are two groups of nerve fibers which are excited by a displacement in opposite directions. Insofar as there are two groups of hair cells, oriented in opposite directions, it is very probable that each nerve fiber innervates the orientated hair cells equally (Flock, Wersall, 1962; Gorner, 1963). Gorner (1963) showed that in each nerve fiber the afferent discharge frequency is greatest when the stimulating direction is parallel to the orientation of the hair cells, since it is only slightly higher than the frequency of spontaneous discharge if the direction of stimulation is perpendicular to this orientation. However, he ascribes this difference in the direction of stimulation not to the directional sensitivity of the sensory cell, but to the mechanical characteristics of the cupula, which is asymmetrical in the animal that he investigated (the frog Xenopus laevis). Békésy (1953) stimulated the hair cells of Corti's organs, applying the vibrating needle to the membrane tectoria. He discovered the negative phase of microphone response corresponding to a shift of external hair cells in the direction of Hensen's cells, and the positive phase to a shift in the direction of the spindle. The directivity pattern approximately, but not precisely, corresponded to two circles. External hair cells were oriented so that the centriole was turned toward Hensen's cells (Flock, et al., 1962; Engstrom et al., 1962). Although basically the external hair cells were oriented in the direction of Hensen's cells, there are deviations in orientation analagous to those seen in the lateral line organ (Flock et al., 1962). Consequently it is very possible that a deviation of the directivity pattern from a circle, observed by Békésy, has the same explanation as the one proposed by Flock (1965) for the lateral line organ. Thus with any direction of stimulation there is always a displacement vector component which corresponds to the orientation of a single hair cell and defines the value of the microphone potential. The fact that the directivity pattern does not precisely correspond with the cosinusoidal function, does not refute this conclusion.

In Figure 12b it is demonstrated that while the value of static displacement of the cupula does not exceed the amplitude of oscillation, the peaks upwards of the directional peaks of microphone response touch the base line corresponding to the value of the rest potential. Positive peaks "break away" from the base line, and a shift in potential arises only when the inclination of the sensory cells is greater than the amplitude of oscillation. But the experiments of Kuiper (1956) and Flock (1955) show that with

oscillation of the cupula around the position of equilibrium, there is a slow negative shift of potentials which is superimposed on the microphone response. Therefore a negative shift in potential is /39
not connected with static displacement of the cupula or with a unilateral inclination of the sensory cells. In the cochlea a similar negative summary potential was observed, but under certain conditions it can be positive (Davis, et al., 1958). In the cochlea, changes in the potential of different signs are due both to static displacement in opposite directions and to oscillations (Tasaki et al., 1954; Békésy, 1953) and reflect a deflection of sensory cells in specific directions. In the lateral line organs the electrical effect of vibrational and static displacement are also closely interconnected and correlate with the directional sensitivity of a single hair cell. Displacement of the cupula, by which the hairs are bent in the direction of the kinocilia, leads to depolarization, and displacement in the opposite direction causes hyperpolarization.

In the lateral line organ, the stimulus-reaction relationship of the hair cell is a nonlinear function in which, as Flock assumes (1965), with a symmetrical vibrational bending of the sensory hairs, the amplitude of negative response is greater than the positive one. If these changes in potentials are integrated in time, then we will obtain a negative shift in potentials. It is assumed that the negative shift in potential observed in symmetrical oscillatory stimulation of the lateral line organs is created by the nonlinearity of the transmission function of the hair cell and is caused by the action of the cellular integrating mechanism, which sums the available microphone potential in time.

Potentials of Receptor Elements and Their Change Under the Action of Alternating Linear Accelerations

In this section we will present the results of our own investigations with intracellular registration of potentials of sensory cells and impulse activity of nerve endings in the utriculus and sacculus, both at rest and with the animals in motion.

Experiments[2] were completed on 12 narcotized (chloralose 40 mg/kg + nembutal 10 mg/kg) cats and 25 pike (without narcosis).

The cat's head was held firm by conducting one malar holder of a sterotaxic instrument (fixed on an oscillating stand) to the vault of the skull, preliminarily cleaned of parietal muscles; the other holder was connected to the surface of the palate. Occular holders lead: (1) to the inner surface of the upper front teeth;

[2] B. B. Yegorov took part in conducting the experiment.

(2) to the edge of the orbit. Thus the position of the animal on the stand was on its side (Fig. 14).

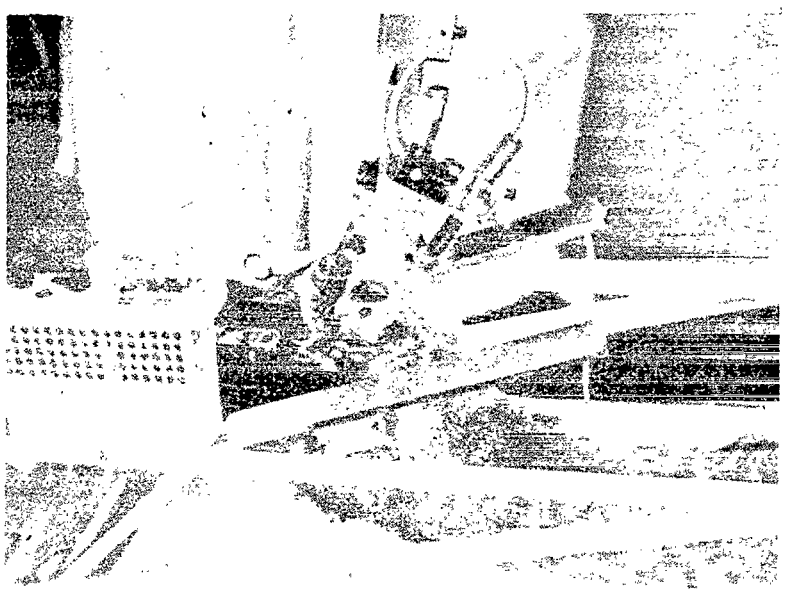

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Fig. 14. Position of the Animal on the Oscillating Stand. The External Chassis of a Direct Current Amplifier "Disa" and the Feeding Part of a Micromanipulator, Fixed to the Frame of a Sterotaxic Instrument.

The concha auriculae with its adjacent muscles was separated from the animal held in this position; then with sharp optic scissors the bulla ossea was sectioned, and under the control of an MBS-2 stereoscopic microscope the lacertus was cut through between the foramen rotundum and the foramen ovale. After a sufficient removal of bone with a fine hook from behind and in a medial direction from the foramen ovale the bubble of the utriculus was found. If the utriculus was injured during the operation, then its walls fell together and it was no longer visible in the microscope; upon leading a microelectrode to it, bio-electric activity could not be registered.

Holding the pike was accomplished by conducting ear holders for rabbits to the branchial bones and by a supplementary fixing of both jaws. At the time of the experiment, every 3-5 minutes water was passed along a rubber tube introduced into the oral cavity. After opening the pectoral bones of the skull at 2-3 mm in a lateral direction from the central line, formations of the vestibule of comparatively large sizes were found: utriculus 1.5 x 1.5 mm; sacculus 2.5 x 2.5 mm.

Potentials of the sensory epithelium were picked up by a glass microelectrode filled with 3 M solution of Cl. /41

Impulse activity of the nerve ending was registered with the aid of a UBT amplifier 1-0.1; intracellular potentials were registered with a direct current amplifier made by "Disa Electronics", having an insignificant zero drift, a grid current less than $\pm 10^{-12}$A, input resistance 10^{12} ohm, input capacitance 50 pF (possibly less by 50 times), maximum compensating capacity 200 pF, upper limit of dynamic band 200 Mohm, transmission band 8 MHz.

Mechanical static arising during the vibration (which was made in the vertical plane) was removed by "cut-off" frequencies lower than 150 Hz.

With intracellular leads (electrode resistance 50 - 100 Mohm) the external chassis of the "Disa Electronics" direct current amplifier was fixed to the vibration stand, whereby the wires from the electrode to the amplifier were insulated and maximally short. With registration in the region of the macula utriculus in cats, we did not once succeed in registering any spontaneous activity, although in fish it was always found.

An insignificant displacement of the stand or movement of the experimentor in the room caused a noticeable appearance of rhythmic activity in the form of activity potentials of amplitude on the order of 250 μV.

With any change of the animal's position in space the interval between the impulses was the same (Fig. 15). In the given figure it is apparent that the impulse activity in the nerve endings of the left utriculus is activated with various changes in the position of the animal. However, the most pronounced changes were observed with changing the position of the animal in the vertical plane. With an increase in the vibration amplitude the frequency of impulsation increased (Fig. 15c and d). Analogous changes were observed for fish.

The facts we obtained indicate that the same nerve ending of the utriculus responds simultaneously to forward, backward and lateral inclinations (cf. Chap. 2). We did not succeed in obtaining any distinct regular laws of change in impulse activity in the macula sacculus (4 experiments) with vibration.

As was noted above, the experiments were conducted with the cats on their side, which caused a displacement of otoliths to the medial plane. Possibly the absence of spontaneous activity is explained by the corresponding polarization of the hair cells in the region of the macula utriculus to which we attached the electrode. The endolymph of the utriculus in the condition of rest had, relative to the perilymph, a potential of 20-25 mV.

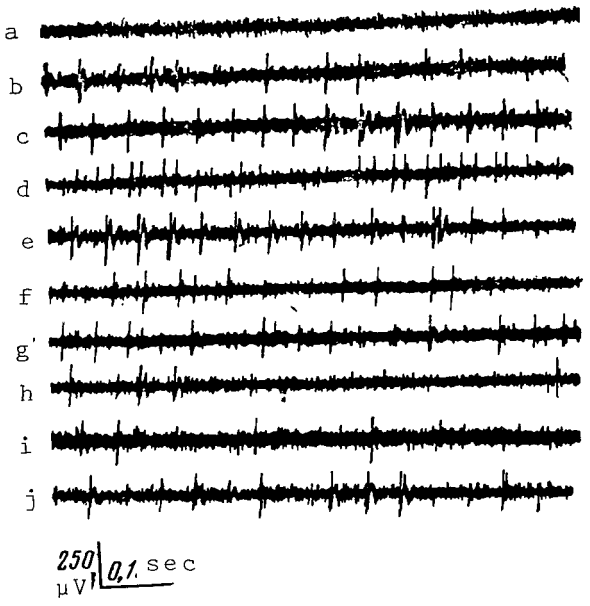

Fig. 15. Change of Impulse Activity of the Nerve Endings of the Left Utriculus with Various Shifts in Position of the Animal (Cat).

(a) Original Picture; (b) Activity with Motion of the Experimenter in the Chamber; (c,d) With Vertical Vibration with an Amplitude of Motion of the Stand 10 and 25 cm; (e,f) With Inclination in the Frontal Plane by 45° Respectively Left and Right; (g,h) Inclination of the Head from the Original Position Down and Up; (i,j) With Turning the Stand into Horizontal Plane Counterclockwise.

Upon conducting the electrodes in the direction of the macula a negative jump in potential on the order of 38 mV (one cell), 40 mV (four), 42 mV (one), 45 mV (four) and 46 mV (one) was noted. An increase in potential in the last case probably was caused by puncture of the sensory cells. The absence of a morphological control did not permit us, however, to categorically confirm that the registered potentials were potentials of only the sensory cell and not of the supporting cell as well. /42

With the animal on its side the rest potential was stable. A change in the animal's position in the vertical plane caused a change in potential in 7 of the 11 registered cells. With each vibration a depolarization on the order of 10 mV arose, having relatively sharp ascending components and a sloping descending component.

We did not succeed once in registering potentials of activity with intracellular leads. /4

It is possible to assume that in the sensory cell of the vestibular apparatus only a receptor potential arises.

The absence of a reaction in 4 cells can be explained by the corresponding polarization of the macula (cf Chap. 2).

Registration of potentials with intracellular leads in pike from the region of the macula utriculus was successfully accomplished only two times, inasmuch as the microelectrode, upon being fed up to the macula, broke by hitting the otolith. Changes of rest

potential with vibration were in no way different from those which were observed in cats.

Comparative morphological investigations of the sensory epithelium of the terminal vestibular organs established a single principle of cellular and subcellular organization of the epithelium.

The sensory regions consist of receptor cells which, together with supporting cells, form a sensory epithelium, innervated by peripheral branches of nerve fibers of the vestibular nerve.

Receptor elements of the ampullas of semicircular canals, utriculus and sacculus, as well as the lateral line organ of fish, are represented by hair cells which are related to mechano-receptors. On the upper surface of each receptor cell are located hair bundles (50-70-100 sterocilia and 1 kinocilium) which project into the cupula or the otolith membrane. A kinocilium always occupies a specific topographical position, which creates morphological asymmetry of the cell; i.e., morphological polarization.

Displacements of the cupula or the otolith membrane by means of hairs are transmitted by the hair cells. In response to stimulus, the receptor mechanism of the hair cell regulating the flow of impulses in the innervating fiber is activated. With an adequate stimulus for the sensory cells a tangential ("cut-off") displacement of the cupula (otolith membrane) in relation to a sensory epithelium appears. A displacement of the cupula is defined by the mechanical characteristics of the cupula, which are simultaneously elastic and plastic. The substance of the cupula is secreted by cells of the epithelium planum semilunatum, of the transition epithelium and the supporting cells. All these elements also take part in the secretion of endolymph. One of the basic components of endolymph is mucopolysaccharides. The correlation of the concentrations of K^+ and Na^+ in the endolymph and an analogous correlation of concentrations of these ions in the intracellular fluid continues to remain enigmatic. /44

The sterocilia act as levers which transmit the mechanical energy of the stimulus to the apical zone of the hair cell, where the roots of the sterocilia are located in the cuticular lamina. Consequently, they are included in the initial stage of the sensory perception process in the sensory cell, which leads to the activation of the bioelectric receptor mechanism. As a result of inclination of the cells, the sensory cell generates a gradual receptor potential, the value of which is proportional to the amplitude but not to the speed of displacement of the cupula (otolith membrane).

Vibration stimulation causes alternating changes of potential, i.e. a microphone potential, the frequency of which is equal to the frequency of the stimulus. This potential is registered both extra-

and intracelullary. The character of the microphone potential changes with a static displacement of the sensory hairs. For the lateral line organ of fish it is not known whether a static displacement causes a stable shift of potential as in other organs belonging to the acoustical lateral system.

The electrical energy of microphone potential is greater than the mechanical energy of the stimulus, and consequently the microphone potential appears not as a purely physical phenomenon, but as an electrical expression of a truly biological sensory process which is connected with the metabolic activity of the organ.

The response of the hair cell depends on the direction of inclination of a sensory hair bundle. This sensitivity is correlated with the morphological polarization of the hair cell, defined by the asymmetrical position of the kinocilium in the sensory hair bundle. The inclination of sterocilia in the direction toward the kinocilium causes depolarization, since inclination in the opposite direction is accompanied by hyperpolarization. With other directions of stimulation, the amplitude of the generated receptor potential is proportional to a displacement vector component parallel to the rows of sterocilia. Directional sensitivity of the cell is indicated by the position of the kinocilium as well as by its asymmetrical superstructure. However, the very same correlation can apply to the gradual growth of sterocilia, to the structure of sterocilia and their roots and to the structure of a particular lamina. At the present time it is difficult to judge on exactly what structure the directional sensitivity of the hair cell depends.

With equal displacements of hair bundles in opposite directions, the value of the produced depolarization is greater than the value of hyperpolarization. The transmission input-output function consequently appears to be nonlinear, at least with amplitudes of oscillation greater than 0.1 μ.

Vibrational stimulation causes a negative shift in potential /45
which is superimposed on the microphone response. This shift in potential is not caused by the constant inclination of the sensory cell. Its appearance can be explained by the nonlinearity of the transmission input-output function, if the alternating microphone potential is summed in time by the cellular integrating mechanism.

Consequently the hair cell possesses a receptor mechanism which registers a stimulus with the aid of changes in electrical potential. The character of the stimulus is reflected in the amplitude at the sign of the receptor potential corresponding to the amplitude and the direction of displacement of the cupula. The nature of the receptor mechanism, which directs the generation of receptor potential, is still unknown, and it is also unknown with which structure it is connected.

CHAPTER II

MECHANICS OF THE VESTIBULAR APPARATUS AND THE PHYSIOLOGY OF THE VESTIBULAR NERVE

Brief Information on the Anatomy of the Vestibular Nerve

The inner ear is innervated by the 8 pair of cerebrospinal nerves, i.e., n. statoacousticus. This nerve emerges from the medulla oblongata at the rear border of the pons Varolii, back of the olive, near the point of emergence of the facial nerve. The nerve is surrounded by hard arachnoid membranes, enters together with the facial and the intermediate nerves accompanied by the internal auditory artery and vein in the internal acoustic meatus. /46

In the acoustic meatus the eighth nerve is separated into the vestibular (n. vestibularis) and the cochlear (n. cochlearis) branches. N. vestibularis forms, in the internal acoustic meatus, a fairly large knot, the ganglion vestibularis (Scarpae).

In animals the lower branch of the vestibular nerve is discerned which has two subsections: to the ampulla of the rear semicircular canal and the saccular nerve, and the superior, which is divided into nerves to the ampulla of the horizontal semicircular canal, to the ampulla of the forward semicircular canal and to the utriculus (Fig. 16).

Lorente de No (1926) and Poljak (1927) distinguished three types of fibers inside the vestibular nerve:fat, medium and thin. Defining the spectrum of diameters of these fibers in man, Engstrom and Rexed (1940) found that 88.5% of the fibers had a diameter of from 2-9 μ and only 4.2% were thinner than 2 μ. Gracek and Rasmussen (1961) present the following data of the spectrum of diameters of the myelin fibers of the vestibular nerve in the guinea pig, cat and monkey; in the cat 38% of the fibers with a diameter from 1 to 2.5 μ, 50% from 2.5 to 5.0 μ, and 12% from 5 to 10 μ; in the monkey 38% with a diameter from 1 to 3.8 μ, 42% from 3.8 to 5.0 μ, and 20% from 5 to 9.0 μ; in the guinea pig 51% from 2.5 μ and less, 42% from 2.5 to 5 μ, and 7% from 5 to 8 μ.

In man the general number of fibers is from 14,000 to 24,000 (A. Rasmussen, 1940).

Concerning the peripheral distribution of various types of fibers the careful investigations of Lorente de No (1926) and Poljak (1927) respectively on mice and man gave compatable results. These results can be summarized in the following way: the thickest fibers supply the peaks of the crista and chiefly the oral portions of the maculae. Each thick fiber is subdivided into a small number of ramuli (2-4) ending around the pase of the pitcher-shaped sensory cells (the scythoid endings). The fibers of average thickness provide chiefly the peripheral portions of the cristae and maculae and in somewhat smaller calexes and the calexes formed by thick fibers (Poljak, 1927), but they additionally form an intraepithelial plexus. These fibers have a sufficiently broad distribution and significant amount of overlapping is observed, (Lorente de No, 1926). The thinnest fibers are scattered on all the sensory epithelium (Poljak, 1927) and end in the form of an intraepithelial plexus of thin fibers. /47

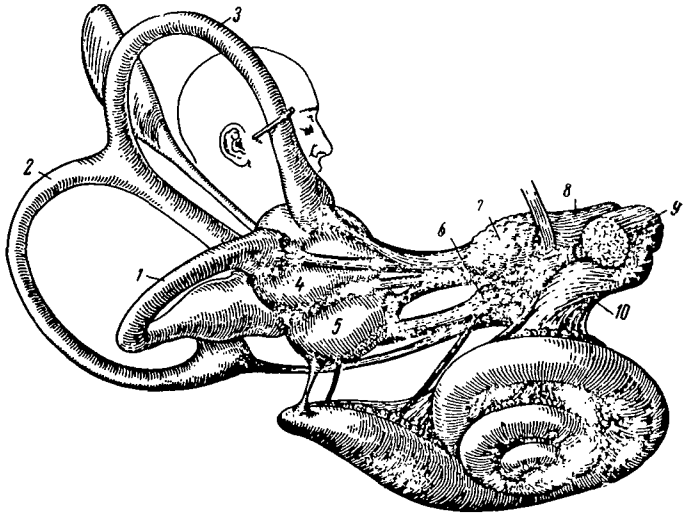

Fig. 16. Subdivisions of the Vestibular Nerve and the Location of the Labyrinth in the Human Skull. Form of the Labyrinth in the Direction Indicated by the Arrow I: 1,2,3, Respectively, the Horizontal Rear and Foreword Semicircular Canals; 4. Utriculus; 5. Sacculus; 6. and 7. Upper and Lower Scarpa's Ganglions; 8. Vestibular Nerves; 9. Facial Nerve; 10. Cochlear Nerve (Weaver, 1965).

Petroff (1955) observed that all the thin fibers which are normally contained in the sensory epithelium of the vestibular apparatus of the cat, disappear in 10-20 days after section of the vestibular nerve. After a short period of survival there can be found signs of degeneration in these fibers. On the basis of his own data Petroff (1955) concluded that these fibers are efferent. /48

TABLE 3. THE NUMBER OF FIBERS IN THE VESTIBULAR NERVE AND ITS BRANCHES (Gacek, Rasmussen, 1961)

Type of Animal	Lower Vestibular Nerve		Upper Vestibular Nerve					
	To the Ampulla of The Rear Canal	Saccular Nerve	To the Ampulla of the Horizontal Canal	To the Ampulla of the Forward Canal	To the Utriculus	Voight's Anastemosis	Trunk of the Upper Vestibular Nerve	Vestibular Nerve as a Whole
Guinea Pig	1522	1260	1592	1797	1703	272	5449	8231
Cat	2585	1821	2269	2453	2694	268	7970	12376
Monkey	3836	2634	3840	3510	3537	296	11801	18271

According to Gacek (1960) the number of efferent vestibular fibers is not great (around 200) in comparison with the general amount (around 12,000) of fibers in the entire vestibular nerve of the cat.

The study of the nuclei of the efferent system of the eighth nerve of guinea pigs and rabbits was conducted anatomically, embryologically and histochemically (Rossi, Cortensina, 1963). In this way it was established that there are 5 bundles of fibers in the composition of the efferent vestibular and cochlea systems. Two of these exist from the upper olive complex, the third from the cells of the reticular formation of the medulla oblongata, the fourth from a group of the lateral vestibular nucleus and the fifth from a nucleus not previously described, designated as the intermediate vestibular nucleus. This nucleus is situated dorsal and medial of the cranial portion of the lower vestibular nucleus and ventral of the caudal portion of the latter nucleus and consists of 100 to 170 multipolar cells with long dendrites. Of these 5 bundles of fibers, 4 are straight and 1 (the first) is crisscrossed (Fig. 17).

The study of retrograde degeneration of bundles after the destruction of the cochlea and the various portions of the labyrinth show that basically the first and second bundles innervate the cochlea, the third the cochlea and the rear labyrinth, the fourth and the fifth are directed to the macular and ampullar sensory epithelium.

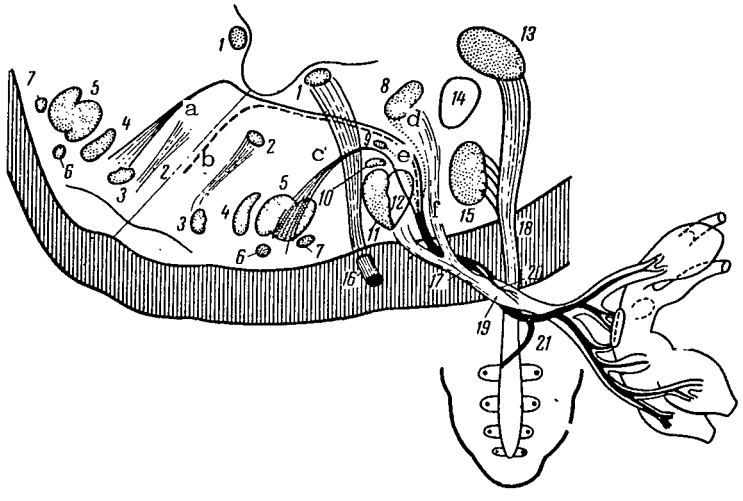

Fig. 17. The Efferent, Cochlear and Vestibular Systems. (1) The Knee of the Facial Nerve; (2) The Nucleus and Fibers of n. abducens; (3) The Nucleus of the Trapezoid Body; (4) Accessory Nucleus of the Olive; (5) Superior Lateral Nucleus of the Olive; (6) Medial Preolive Nucleus; (7) Lateral Preolive Nucleus; (8) Lateral Vestibular Nucleus; (9) Intermediate Vestibular Nucleus; (10) Inferior Vestibular Nucleus; (11) Nucleus and Descending Root of the Trigeminal Nerve; (12) Descending Root of the Trigeminal Nerve; (13) Dorsal Cochlear Nucleus; (14) Striated Body; (15) Ventral Cochlear Nucleus; (16) Facial Nerve; (17) Vestibular Branch of the Eighth Nerve with 2 Roots Superior and Inferior; (18) Cochlear Branch of the Eighth Nerve; (19) g. Scarpa; (20) Small Bundles of Efferent Fibers, Which End at the Level of g. Scarpa; (21) Oort's Anastomosis; (A) Intersecting Efferent Cochlea Bundle; (B) Direct Reticular Bundle; (C) Direct Efferent Cochlea Bundle; (D) Direct Dorsal Efferent Vestibular Bundle; (E) Direct Ventral Vestibular Bundle; (F) General Bundle of Various Groups of Efferent Fibers (Rossi,Cortensina, 1963). /49

Mechanics of the Semicircular Canals and Physiology of the Ampullar Nerve

At first the mathematical description of the physical phenomena, taking place in the semicircular canals with rotational movements, was given by Mach (1874), Gaede (1923) and in 1926 by Rohrer and Masuda. At the time nothing was known about the mechanical characteristics of the cupula and naturally these characteristics were not reflected in the equations of the movement of the endolymph given by the authors.

Steinhausen (1931) in excellent experiments on live pike showed that the cupula as a whole overlaps the ampulla of the semicircular canal, and having passed from the position of equilib-

rium under the action of its own elasticity it slowly (20 seconds and greater) returns, pushing endolymph before it. This principle

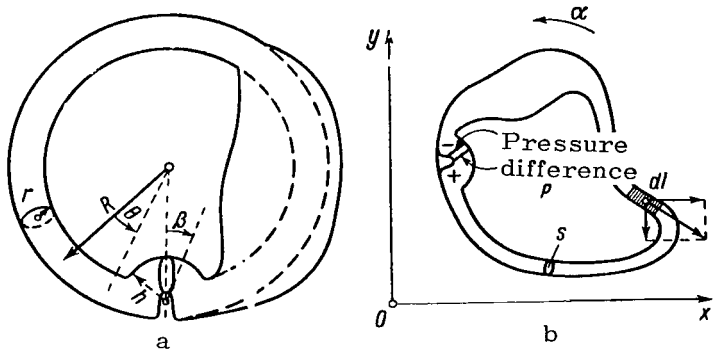

Fig. 18. Influence of the Form of the Semicircular Canal Upon its Function. (a) A Semicircular Canal of the Correct Round Form; (b) A Canal of Derivative Form, Rotating With Angular Acceleration α Around an Axis Passing Through the Zero Point (Groen, 1956). /50

important observation, repeated later by Dohlman (1935) permitted Steinhausen (1933) to advance a hypothesis that the cupulo-endolymphatic system must be considered to be a single mechanical system possessing the characteristics of a twisting pendulum with great friction. It is interesting that Schmaltz (1932), who met with Steinhausen and saw his experiments, did not consider the elastic forces of the cupula in his precise mathematical analysis of the motion of the endolymph.

The theoretical development and comprehensive experimental testing of the Steinhausen hypothesis is found chiefly in the works of the Utrecht school of investigators (van Egmond, et al., 1949, 1952; Groen et al., 1952; Groen, 1956, 1957; Hartog, 1963).

With this conclusion, equations of the endolymph motion in the semicircular canal proceeded from the following assumptions:

(1) The semicircular canal is a closed canal entirely filled with a homogeneous viscous noncompressible fluid;

(2) A cross section of the ampulla of the semicircular canal is completely overlapped by the weightless elastic cupula, subject to Hook's law;

(3) The viscous and elastic characteristics of the cupula endolymphatic system are unalterable;

(4) Component velocities of the endolymph in a cross section of the canal can be considered to be small;

(5) The rotation of a semicircular canal of the correct ring shape (toroidal) around the axis is considered, passing through the center of a circle bounded by the canal (Fig. 18a). /51

The latter assumption is not obligatory (Bauminger, 1941;

van Egmond et al, 1952, de Vries, 1956; Groen, 1957; Weaver, 1965). Actually, suppose that a canal of the derivative shape revolves counter-clockwise with an angular acceleration α around an axis perpendicular to the plane of the canal in passing through the zero point (Fig. 21b). The endolymph in the semicircular canal will begin a motion in the reverse direction relative to the walls of the canal, creating along one side of the cupula a region of elevated pressure, along the other a region of lowered pressure. We will consider the element of the tubule $d\vec{l}$ with coordinates of the center of gravity X and Y relative to the center of rotation. The projection dl on the abscissa axis is dx, on the ordinate axis dy. The X-component of force acting on this fluid element can be presented in the expression $+\alpha y \rho s dx$, and the Y-component by the expression $\alpha x \rho s dy$, where ρ is the density of endolymph and s is the cross section of the canal. Then the drop in pressure on the cupula will be defined by the contour integral

$$P = \alpha\rho \oint y dx - x dy = 2\alpha\rho \sum, \tag{1}$$

Σ is the area bounded by the canal.

Thus, neither deviations from the ideal ring-shape, nor distribution of the axis of rotation has an influence on the drop in pressure and consequently on the motion of the endolymph if the area bounded by the canal remains constant.

Having represented the semicircular canal in the form of a section of a tubule closed at the ends, in which a flow of fluid is absent, Morgan et al. (1943) came to the conclusion that the reaction depends upon a location of the axis of rotation. It is necessary to note that an expression for the drop in pressure obtained by these authors is automatically converted into form (1) if we turn the tubule into a ring.

With the assumptions enumerated above and in the absence of external perturbing forces, the differential equation of endolymph motion in the semicircular canal is defined by the balance of the moments of the forces of inertia, viscous friction and elastic forces;

$$I\ddot{\theta} + c\dot{\theta} + k\theta = 0 \tag{2}$$

or

$$\ddot{\theta} + \frac{c}{I}\dot{\theta} + \frac{k}{I}\theta = 0, \tag{3}$$

where θ, $\dot{\theta}$, $\ddot{\theta}$ are, respectively, the angular displacement, the angular velocity and the angular acceleration on the endolymph on the axis of the canal relative to its walls; I is the moment of inertia of the endolymph ring, g·cm^2; c is the coefficient of the moment of the forces of friction, g·cm^2/sec^{-1}; k the coefficient /52

of the moment of elasticity forces, $g \cdot cm^2/sec^{-2}$.

Equation (2) describes not only the motion of the endolymph but also the motion of the cupula. Let r be the radius of the canal, R the radius of the ring and θ the angular displacement of the endolymph (Fig. 18). Insofar as the cupula closely abuts the ampulla, then the volume of displaced endolymph in the canal $\pi r^2 R\theta$ and the volume of the endolymph displaced by the cupula, having at the same time turned around to the angle β relative to the center of the crista, $V\frac{\beta}{\pi}$, must be equal then

$$\frac{\beta}{\theta} = \frac{\pi^2 r^2 R}{V}, \tag{4}$$

where V is the volume of the ampulla.

If we assume that the ampulla has a hemispheric form then $V = \frac{4}{3}\frac{\pi h^3}{2}$, where h is the radius of the hemisphere. Substituting this expression and the values $R = 0.3$ cm, $r = 0.003$ cm, $h = 0.1$ cm into formula (4) we obtain $\beta/\theta \approx 1$ (Groen, 1957). We will arrive at the same result using the mean value of the amount $\frac{r^2 R}{V}$, defined by the measurement of the sizes of the semicircular canals on 44 types of animals and equal to 0.0509 ± 0.0264 (Jones, Spells, 1963).

Thus the angular displacement of the endolymph and the angle of rotation of the cupula are not only proportional (which would be sufficient in order that, by a simple change of the angle θ to β, the equation of motion of the endolymph could be converted into an equation describing the motion of the cupula), but are values of one magnitude.

Steinhausen did not define the coefficients I, c and k of the differential equation (1) in pike and therefore could not confirm his hypothesis quantitatively. This was done by Groen and his coauthors (Groen et al., 1952) for the labyrinth of the skate and by Hartog (1963) for the labyrinth of the frog.

An approximate solution of equation (1) for the case of great friction (supercritical damping, $c/I >> k/I$) and with the initial condition $\theta = 0$, $\dot{\theta} = \gamma$ where $t = 0$ such that:

$$\theta_{(t)} \approx \gamma \frac{1}{c}\left(e^{-\frac{k}{c}t} - e^{-\frac{c}{I}t}\right), \tag{5}$$

where e is the base of natural logarithms. If a thrust imparts an angular velocity γ to the endolymph, then the cupula, for a very short interval of time, on the order of 0.1 sec (Groen et al., 1952; Mayne, 1952) will be displaced at an angle

$$\theta_{max} = \gamma \frac{I}{c}. \tag{6}$$

Insofar as damping c of the cupula-endolymph system is considered large, the equation describing the revolution of the cupula from a deflected position into a position of equilibrium will assume the form /53

$$\theta_{(t)} \approx \theta_{max} \cdot e^{-\frac{k}{c} t}. \tag{7}$$

Measuring the angle of deflection of the cupula in the function of time with motion to the position of equilibrium, it is possible to define the ratio k/c.

The representation of the motion of the cupula gives a change in frequency of impulsation in the ampullar nerve. If we assume that the change in frequency of the nerve discharge $\nu_{(t)} - \nu_0$, where ν_0 is the frequency of spontaneous impulsation proportional to the displacement of the cupula (Morales, 1946; Groen et al., 1952), the curves $\theta_{(t)}$ and $\nu_{(t)} - \nu_0$ must have the same shape. Then

$$\nu_{(t)} - \nu_0 \approx (\nu_{max} - \nu_0) e^{-\frac{k}{c} t}, \tag{8}$$

or

$$t \approx \frac{c}{k} \ln \frac{\nu_{max} - \nu_0}{\nu_{(t)} - \nu_0}. \tag{9}$$

Hence it follows that a graph of the change of frequency of impulsation in the ampullar nerve as a function of time, constructed in a semi-logarithmic scale, will be a straight line; the tangent of the angle of inclination of which, through the logarithmic axis, is equal to c/k.

The differential equation of motion of the endolymph for the case, when the semicircular canal is subject to harmonic angular oscillation in the same plane has the form

$$\ddot{\theta} + \frac{c}{I} \dot{\theta} + \omega_0^2 \theta = \omega^2 A \sin \omega t, \tag{10}$$

where $\omega = \frac{2\pi}{T}$ is the angular (or cyclic) frequency, T is the period of harmonic oscillation, $\omega_0 = \sqrt{\frac{k}{I}} = \frac{2\pi}{T_0}$ is the angular frequency, T_0 is the characteristic period or the period of free oscillation of the cupular system, i.e., the endolymph in the absence of damping; A is the maximum altitude, $\omega^2 A$ is the maximum angular acceleration of a fixed point of the canal.

An approximate solution of equation (10) for the case of great friction and where $t \to \infty$ is such that

$$\theta \approx \omega A \frac{I}{c} \sin(\omega t - \varphi), \tag{11}$$

whereby

$$\tan \varphi = \frac{\omega}{\omega_0^2 - \omega^2} \cdot \frac{c}{I}, \tag{12}$$

where ϕ is the phase difference between the displacement of the cupula and the canal.

If the frequency ω of the harmonic oscillations of the canal is equal to the characteristic frequency of the cupular endolymphatic system then from (12) it follows that $\tan \phi = \infty$ and $\phi = 90°$. This signifies that when any fixed point of the canal reaches its maximum angular displacement (speed of the canal at this moment is equal to zero), the cupula passes its position of equilibrium (angular displacement of the cupula equals to zero) with maximum speed. When the same fixed point of the canal passes this position of equilibrium (speed of the canal maximum) the cupula is maximally deflected (speed of the cupula equal to zero). /54

Thus in the case of resonance ($\omega = \omega_0$) the angular displacement of the cupula (change in frequency of infiltration in the ampular nerve) is in phase with the speed of the canal. It is also interesting to note that at any moment the displacement of the endolymph (of the cupula) is proportional to the speed of the canal ωA and not to the acceleration $\omega^2 A$, in which the integrating characteristics of the cupula-endolymph system appear.

Introducing the angle $\psi = 90° - \phi$, equal to the phase difference between the deflection of the cupula (with a change in impulsation) and to the speed of oscillations, we obtain from (12) that

$$\tan \psi = \cot \varphi = \frac{\omega_0^2 - \omega^2}{\omega} \cdot \frac{I}{c}. \tag{13}$$

where $\omega \ll \omega_0 \; (T \gg T_0)$

$$\tan \psi = \frac{1}{2\pi} \cdot \frac{k}{c} \cdot T, \tag{14}$$

the phase difference is positive, and the cupula anticipates a change in the speed of oscillations. Where $\omega >> \omega_0$ ($T << T_0$)

$$\tan \psi = -2\pi \frac{I}{c} \frac{1}{T}, \tag{15}$$

the phase difference is negative, and the cupula lags behind.

Measuring ψ and T, it is possible to calculate the ratio k/c and c/I.

Thus, if the hypothesis of Steinhauser that the cupula-endolymph system must be considered as a super-critically damped twisting pendulum is true, then experiments based on mechanical principles will allow the possibility of defining three values of the relations of the coefficients of the differential equation. The ratio c/k is defined from measuring the changes of impulsation in the ampullar nerve after a jump-like change in the angular velocity of the canal and the ratios k/c and c/I from the measurements of the phase difference between the oscillation of the canal and the cupula, if the frequency of the oscillating motion is greater or less than the characteristic frequency of the cupula-endolymph system. The ratio k/c will appear as a control for the ratio found in the first experiment.

Such experiments with the application of electrophysiological /55
methods for recording action potentials from single fibers of the ampulla nerve of the horizontal semicircular canal were conducted by Groen and coll. (1952) on a preparation of an isolated labyrinth of the thorny skate (Raja clavata).

In the majority of single nerve fibers at rest, a spontaneous impulsation with a constant frequency (total deviation from the average value of 4%) was discovered. Probably each potential was produced only by a single sensory cell, or a group of synchronously impulsing receptors. Upon turning the labyrinth under investigation on its side (ipsilateral angular acceleration) eliciting an ampullopetal current in the endolymph and correspondingly in the utriculopetal deflection of the cupula, the impulsation frequency rose; upon turning the labyrinth from the opposite side, with a contralateral acceleration, eliciting an ampullofugal current in the endolymph (utriculofugal deflection of the cupula), the impulsation frequency fell. A sudden cessation of the turning motion with a constant speed (a "stop stimulus") led to the appearance of a frequency of impulse discharge after the contralateral rotation which, in the given case, corresponds to the utriculopetal deflection of the cupula and to a decrease in frequency after the ipsilateral rotation (utriculofugal deflection of the cupula).

Thus, the deflection of the cupula in the direction toward the utriculus is stimulating for the described type of single nerve fibers, and therefore stimuli producing a similar deflection are called positive. A deflection of the cupula toward the canal is inhibitory and a stimulus eliciting such a deflection is called negative. There are opposite regularities in the vertical canals: a deflection of the cupula toward the utriculus was inhibitory, and a deflection in the opposite direction was excitory.

As a rule, the positive stimulus elicited a larger change in frequency of rest discharge than a negative stimulus of equal volume, although a sufficient number of nerve fibers were found,similarly sensitive to stimuli of opposite directions. This type of bilaterally

sensitive receptor was described in 1940 by Lowenstein and Sand. Ross (1936) probably found them but he did not attribute any functional significance to the rest activity nor to the decrease in activity with ampulofugal current of the endolymph, ascribing these phenomena to experimental errors.

However, there are such sensory units (a single nerve fiber together with all receptors innervated by it) which do not manifest spontaneous activity, "which are silent" in a rest condition and which react only to positive stimuli of large values. Possibly Zotterman (1943) in experiments on pike and burbot, encountered this type of unilaterally sensitive receptor.

It is interesting that in the statocyst of the octopus (octopus vulgaris) in the nerve innervating the longitudinal section of the complex crista, the receptors of which react to angular acceleration in the horizontal plane, all fibers are silent. Impulsation arises only with rotation in the ipsilateral side (Maturana, Sperling, 1963). /56

Diametrically opposite in character are units with an impulsation frequency notably higher than the average, the activity of which remains, in general, unchanged for a broad range of positive and negative stimuli and can only be reduced under the action of a very strong negative stimulus. Probably the single nerve fibers of the ampullar nerve, described in 1940 by Lowenstein and Sand and in 1943 by Zotterman, represent nothing more than this type of unilaterally sensitive receptor. In contrast to bilaterally sensitive receptors in which, as experiments have shown, it is impossible to discover an actual threshold since the slightest angular motion produces a change in impulsation frequency in the nerve fiber, unilaterally sensitive receptors possess a comparatively high threshold.

The described components of functional units do not appear to be absolutely discrete, defining a principle difference between receptors, inasmuch as all intermediate types between them are found.

For the calculation of constants of the differential equation (2), only fibers equally sensitive to angular accelerations of opposite directions are suitable. Actually, from the assumption that the change in frequency of action potentials in the nerve fiber is proportional to the deflection of the cupula and from correlation (6) it follows that

$$\theta_{max} \approx \nu_{max} - \nu_0 \approx \gamma. \tag{16}$$

Plotting this dependency on a graph for each fiber, it is possible to select those which possess equal sensitivity. Figure 19a depicts a curve connecting the value of the stimulus (γ) with the impulsation frequency in a three-fiber preparation of the

ampullar nerve of a skate (Groen et al., 1952). The S-shaped curve has a rectilinear section (the region of constant sensitivity) in a band of stimuli from -40°/sec to +40°/sec, and is quite similar to the known characteristic curves of a triode lamp (Fig. 19b). Here along the abscissa axis is the anode current. In the presence of a signal stress, the anode current is defined by grid displacement. In the proposed analogy (Groen et al., 1952) the value of

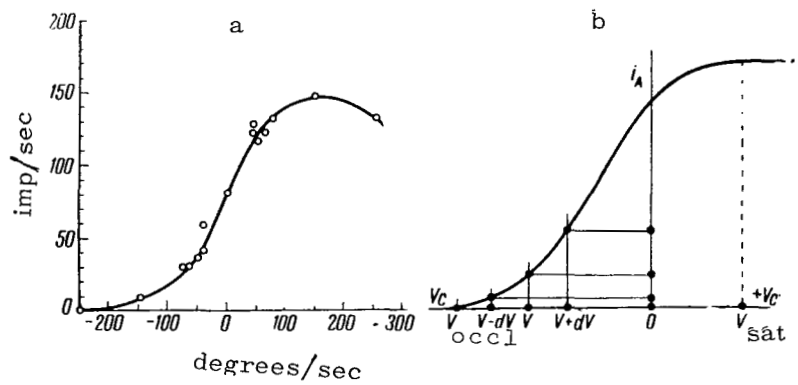

Fig. 19. Characteristic Curves of a Three-Fiber Preparation of the Ampullar Nerve of a Skate (a) and of a Triode Lamp (b) (Groen et al., 1952). /57

the stimulus (in °/sec) corresponds to the signal stress on the grid, the impulsation frequency in the nerve to the anode current and the frequency of spontaneous activity is defined by the "displacement" in that part of the functional unit which is responsible for the conversion of the mechanical stimulus (deflection of the cupula) into a discharge of the nerve fiber impulses; that is, in the membrane of the dendrite fibers encompassing the sensory cell. If the analogy is true, then by changing the grid conditions it is possible to shift the working point (frequency of spontaneous activity) of the receptor unit upwards and downwards along the characteristic curve. Then the working point of a symmetrical bilaterally sensitive receptor would lie in the middle of the rectilinear section of this curve, and equal in strength, but rotational stimuli in the opposite direction would elicit an equal increase and decrease in the frequency of spontaneous impulsation. In a receptor from the working point in the lowest portion of the curve (point of closure, V_{cl}) the spontaneous impulsation is absent; it is silent at rest and reacts only to a positive stimulus which decreases the negative displacement. If the working point is located in a horizontal upper portion of the curve (saturation point V_{sat}), the receptor possesses an elevated spontaneous activity which remains constant over a broad band of accelerations. Only a stimulus decreasing the positive displacement will lead to a change (decrease) in the impulsation frequency. These are receptors

of uni-directional sensitivity possessing a high threshold.

In an investigation of the activity of galvanic polarization on the sensory epithelium of the labyrinth, Lowenstein (1953, 1955) showed, that a current passing through the nerve to the sensory /58
endings (depolarizing the epithelium of the crista) leads to the increase in frequency of spontaneous impulsation, and a current in the opposite direction (hyperpolarizing) decreases or even completely eliminates the rest discharge, whereby the activity of the polarized potential and the response to rotation are summed algebraically. With the aid of a shift of the working point it is possible to convert a symmetrically reacting receptor unit into an asymmetrically working one, and inversely. Thus there is a constant collection of receptor units, differing in initial polarization (displacement) sensitivity (slope of the rectilinear section of the characteristic curve) and the maximum value of impulsation frequency (value of saturation current).

Spoendlin (1965b) further develops the analogy between a triode lamp and the function of nerve units, drawing a parallel between the synapsis of a sensory cell and the apertures in the grid of a cathode lamp. The larger the apertures in the grid and the more of them there are, then with a given stress on the grid the current is stronger from the cathode to the anode. Then differences in the function of silent and spontaneously active units may be associated with the number and state of synapses of the various sensory cells. Silent receptors possessing a high threshold would correspond, then, to sensory cells with a small number of functional synapses. As was discovered, there are sensory cells with a very small number or completely without synaptic structures (Spoendlin, 1956b). In Figure 20 in a semilogarithmic scale a dependency of the change in impulsation frequency of a single nerve fiber after a sudden deflection of the cupula by a stimulus of 36°/sec is presented. In correspondence with theoretical considerations it is rectilinear; the tangent of the angle of inclination of the straight line to the logarithmic axis is equal to 40 and gives a time constant of the cupula-endolymph system c/k.

Figure 21 presents an example of the change in impulsation frequency of a single fiber with sinusoidal motion of the preparation. The points of intersection of the sine curve of the change in frequency with the horizontal line, carried out at the level of frequency of the rest discharge, indicate moments when the cupula passes the position of equilibrium (zero deflection). The vertical broken lines indicate the turning points of the oscillating motion, and the points of their intersection with the sinusoidal curve give the phase difference ψ. Thus, the phase difference calculated from the various preparations is traced in a function of the logarithm of the oscillation period T on Figure 22. Two branches of the curve have asymptotes, whose tangents to the angle of inclination are defined by formulas (14) and (15). Hence c/k = 22 sec, c/I = 36 sec, i.e., ω_0 = 1.3 sec^{-1}.

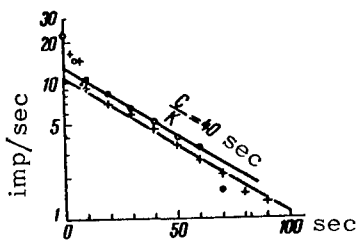

Fig. 20

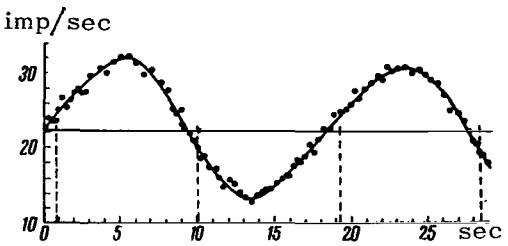

Fig. 21.

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Fig. 20. Change in Frequency of Nerve Impulses in Time with "Stop Stimulus" (Groen et al., 1952).

Fig. 21. Change in Frequency of Nerve Impulses With Sinusoidal Oscillations (T = 18.4 sec, A = 54°, Phase Angle of Advance 13.5 ± 2°). The Revolving Points of the Oscillations Are Indicated by the Dotted Vertical Lines. (Groen et al., 1952).

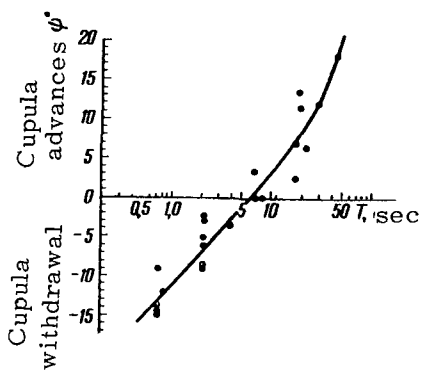

Fig. 22. Phase Difference as a Function of the Period of Oscillation T (Groen et al., 1952).

If the anatomical measurements of the semicircular canal are known, then it is theoretically possible to calculate the ratio c/I. The moment of inertia I is defined by the rings of endolymph, including part of the utriculus (van Egmond et al., 1949), which in Figure 18a is designated by the dotted line

/60

$$I = 2\rho\pi^2 r^2 R^3, \qquad (17)$$

where ρ is the density of endolymph; R is the radius of the ring; r is the radius of the canal.

The coefficient of the moment of forces of friction c can be derived from the Poiseville law insofar as the utricular portion of the canal introduces a small contribution to the moment of forces of friction; the length of the canal of damping will be approximately defined by half the length of the circumferance, that is πR. The volume of the fluid has a viscosity μ, flowing through the canal with

a round cross section of the radius r and the length πR for time t under the action of the constant pressure P equal to the value

$$V = \pi r^4 \frac{Pt}{8\mu\pi R}. \tag{18}$$

From the other side, with an angular velocity of the endolymph of 1 rad/sec (1 rad = 57.3°) for a time t through the canal a volume of liquid will flow:

$$V_1 = \pi r^2 R t. \tag{19}$$

Equating the volumes and performing elementary transformations, we obtain an expression for the pressure necessary to move a fluid through a canal with a volume V_1

$$P_1 = \frac{8\mu\pi R^2}{r^2}. \tag{20}$$

Then the moment of the forces of friction c is defined by the derivative of pressure on area of the cross section of the canal and the radius of the ring

$$c = 8\mu\pi^2 R^3. \tag{21}$$

From expressions (17) and (21) it follows that

$$\frac{c}{I} = \frac{4\mu}{\rho r^2}. \tag{22}$$

Schmaltz (1932) obtained a value 2 times greater since he took the entire length of the canal for the calculation of the moment of inertia and the moment of forces of friction. From a hydrodynamic point of view, a more preferable solution was given by Egmond et al., (1949).

In the skate r = 0.34 mm, ρ = 1 g/cm^3, μ = 0.01 poise, therefore

$$\frac{c}{I} \approx 35 \text{ sec}^{-1}.$$

The true form of the semicircular canal is more complex than that used for calculation, and the value of the viscosity coefficient is quite approximate; therefore a correspondence between the calculated value and the experimental one is perhaps accidental, chiefly due to the fact that these values are of one magnitude. /61

The characteristic curve (Fig. 19a) only in the first approximation describes the function of the receptor, insofar as its response depends not only on the stimulus, acting in the moment of time under

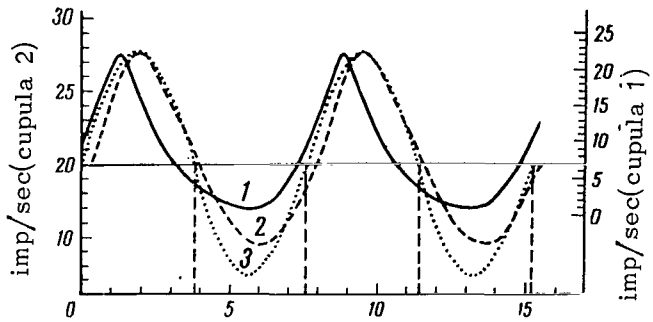

Fig. 23. Change in Frequency of Nerve Impulses in Two Sensory Units of One Preparation With Sinusoidal Oscillations (T = 0.76 sec, ωA = 18°/sec. The Revolving Points of the Oscillating Motion Are Designated by the Dotted Lines. (Groen et al., 1952). (1) Distorted Sinusoidal Curve (Angle of Lead According to Phase 24°); (2) A Less Distorted Sinusoid (Phase Lag 13°); (3) Ideal Sinusoid For Comparison (in Zero Phase).

consideration, but also upon the preceding stimuli. There is a kind of "hysteresis"; an "output" after the inhibitory stimulus, an inhibition of activity after an excitory stimulus, and even a period of nonexcitability or silence. The general physiological principle of post-stimulatory inhibition of activity and post-inhibitory increase ("output") was observed in the experiments of Groen et al., (1952). Thus, after a test of revolution with stop stimulus, the frequency of rest discharge often changed in comparison with discharge before rotation.

The response of the receptor unit to vibratory shaking sometimes presented a clearly distorted sinusoid. In Figure 23 the change in frequencies of two receptor units of one preparation is shown. One gives a strongly distorted sinusoid with an angle of lead according to phase, although lag was expected (Curve 1). A response of the second unit is less distorted (Curve 2), and is much closer to a true sinusoid (Curve 3).

The receptor units with a clearly expressed hysteresis were /62 not taken into consideration for deriving the constants, but insofar as the phase differences obtained with harmonic oscillation of the preparation were quite small, the distortion of the sine response with hysteresis has a substantial influence on the measurement which is seen in Figure 23. Probably, in a large number of experiments hysteresis leads to increased phases of angle of lead and decreased phases of lag. According to expressions (14) and (15) this will give decreased values of c/k and increased values of c/I. Hysteresischanges even the value c/k obtained in experiments with

stop stimulus. However if the influence is limited primarily by frequencies measured directly after stopping, then the cupula is maximally deflected. These frequencies were not taken into consideration for the definition of deflection (cf. Fig. 20). But in this experiment nonlinearity of receptor reactions has important significance. Insofar as in the majority of receptor units the working point is located in the lower portion of the characteristic curve (the point V_{cl}, Fig. 19b), nonlinearity leads to a decrease in the constant k/c in expression (7) for the stimulus, producing a decrease in the impulsation frequency. Thus, c/k obtained in these experiments will be somewhat increased. The influence of nonlinearity on the deflection of the curve after the excitory stimulus (ampullopetal current) is of the opposite character but usually much smaller.

The correspondence between the results obtained in experiments with stop stimulus and with sinusoidal vibration of the semicircular canal, and theoretically with the calculated values taking the possible systematic errors into account, is sufficiently good.

It is possible to consider that Steinhausen's pendulum theory was confirmed experimentally. The differential equation describing the motion of the endolymph (or the cupula) in the "mean" skate labyrinth, is such:

$$\ddot{\theta} + 35\dot{\theta} + \theta = 0. \qquad (23)$$

It is natural that the function of the entire ampullar nerve, consisting of the described types of single nerve fibers, is very similar to that of bilaterally sensitive fibers. Thus, all authors who registered ampullar nerve activity noted the presence of spontaneous activity. With the action of positive stimuli, the impulsation frequency in the ampullar nerve of the horizontal semicircular canal increases; with the action of a negative stimulus, it decreases, indicated by the investigations of Lowenstein and Sand (1936) on the nerve of a shark and in 1940 on the nerve of a skate, Ledoux (1958, 1960), Hartog (1963) on the nerve of a frog, Owada and Kimura (1960) on the ampullar nerve of a horizontal canal of a rabbit.

The dynamic response of a semicircular canal to rotation undoubtedly depends upon the completeness of the structure of the whole labyrinth. Any injury which leads to destruction of the continuity of the labyrinth and the circulation of the endolymph inside the canal prevents dynamic responses. Thus, an isolated labyrinth /63
in a skate (Lowenstein, Sand, 1940b) prepared by bandaging a severed semicircular canal or a perforated sacculus ceased to react with excitations or inhibition to angular displacements. Spontaneous discharge appears as a characteristic quality of the acoustical lateral receptors which does not depend upon special structural characteristics of the labyrinth. It exists while the sensory unit of the crista are intact and are in good physiological condition.

The same complete structure of the semicircular canal, ampulla and cupula defines and limits the mechanical conditions which elicit deformation of the canal and a consequent change in frequency of discharge in the nerve.

With a deflection of the cupula a change in impulsation frequency in the whole nerve, because of the presence of unidirectional fibers which are silent at rest in its composition, will be greater than in a single bilaterally sensitive fiber. Consequently even the characteristic curve of the nerve will be shorter than the characteristic curve of the fiber (Ledoux, 1949, 1958; Hartog, 1963). Restoration of the same frequency of action potentials of the nerve to the value of spontaneous frequency with the motion of the deflected cupula in a position of equilibrium due to the exclusion of silent fibers will take place more quickly (k/c is greater) than in single bilaterally sensitive fibers. Correspondingly the value of c/k obtained from multifibered preparations will be lower (Groen et al., 1952).

Thus, coefficients obtained in experiments on an isolated preparation of a labyrinth with the registration of action potentials of the whole nerve reflect "viscous elastic" characteristics of a more complicated system: the "cupula-endolymph-ampullar nerve". The differential equation of such a system for the average frog labyrinth obtained by Hartog (1963) has the form

$$\ddot{\theta} + (139 \pm 20)\dot{\theta} + (35 \pm 29)\theta = 0 \qquad (24)$$

This equation is correct for stimulus values in the band of $\pm$ 30°/sec. Outside of this band the linear connection between the change in frequency of the nerve and the deflection of the cupula is destroyed, and simultaneously phenomena of post-inhibitory output and post-excitory inhibition arise. Thus there is a physiological limit to the applicability of the equation.

We will compare the different characteristic curves of the stimulus: the cutting force acting on the surface of the crista, the change in potential inside the sensory epithelium (Trincker, 1957), change in frequency of action potentials of a single nerve fiber (Groen et al., 1952) and a change in the mean amplitude of the mass discharge in the entire ampullar nerve (Ledoux, 1958).

The curve connecting the change in rest potential of the angle /64 of deflection of the cupula is S-shaped and recalls the sinusoid of cutting force (Fig. 24), whereby the range of physiologically important deflections of the cupula corresponds near to the steep linear central section of the curve.

The S-shaped curve of the change in frequency has a steeper slope and corresponds only to the central section of the receptor curve.

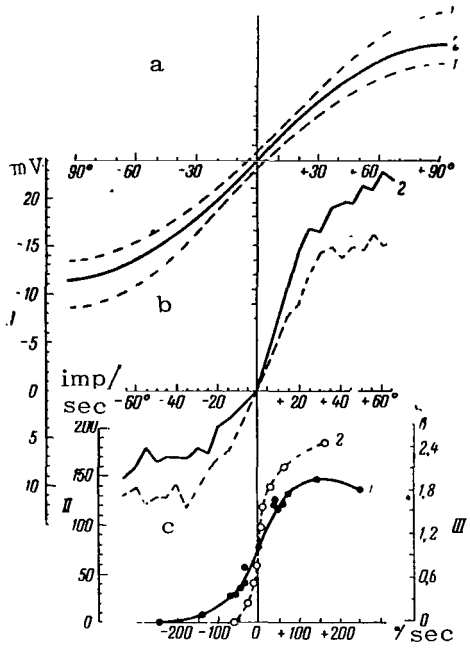

Fig. 24. Characteristic Curves of the Receptor System of the Semicircular Canals (Trincker, 1962). (A) Cutting Force Acting on the Sensory Epithelium of the Crista with Deflections of the Cupula (1) Mean Zone of the Surface of the Crista, (2) Lateral Surfaces); (B) Change in Rest Potential Inside the Layer of Hair Cells of the Crista of the Horizontal Semicircular Canal of a Guinea Pig (I Potential Differences Arising with Deflection of the Cupula and the Rest Potential); (C) Connection Between Frequency of Action Potential (1. Ordinate II) in a Three-Fiber Preparation of the Ampullar Nerve of a Skate, Summary Amplitude of Action Potentials (2. Ordinate III) of the Whole Ampullar Nerve of a Frog and the Value of "Stop Stimulus".

A still greater increase in steepness observed in the characteristic curve of mass discharge is explained by the collection of units silent at rest with the increase in the value of stimulus.

Bilateral changes in the rest potential of the sensory epithelium, and correspondingly superior and inferior modulation of spontaneous impulsation of the first neuron, begins from the working point located in the middle of the rectilinear section of the characteristic curve, which ensures that the terminal organs of the semicircular canals are very highly sensitive to angular accelerations.

It is necessary to note that although at the present time the activity of the ampullar nerve and of single fibers in warm-blooded animals has not been analyzed as carefully as in cold-blooded animals, there is little probability that the labyrinth of warm-blooded animals essentially differs in function from the labyrinth of the lower vertebrates (Lowenstein, 1956; Gernad, Gilman, 1960a), to which the above-mentioned report of Ovada and Kimora (1960) testifies. /65

Electrophysiological experiments on the preparation of the isolated labyrinth of a thorny skate still showed that the semicircular canal does not react to gravitational nor consequently to any other linear accelerations. This result is supported by the

data of Wilstrup (1951a), who studied the inertial characteristics of the cupula in living sharks (Acanthias vulgaris). It is found that with physiological values of accelerations, the inertia of the cupula was insufficient to overcome its resistance to motion and to cause motion along the crista. Only by artificially weighting the cupula with mercury or with a column of endolymph 3-4 mm long (diameter of canal 0.8 mm) was it possible to displace the cupula. Also it must be noted that Parker and von Gierke (1965) with centrifugation of guinea pigs at an acceleration of 100-400 g did not observe any detachment of the cupula from the crista. On the other hand, Gernandt (1950), introducing a microelectrode into the eccentrically positioned head of a cat along the vestibular part of the eighth nerve at a portion between the internal acoustic passage and the medula oblongata, discovered a change in impulsation in the fibers supposedly innervating the crista of the horizontal canal. It is possible that this is explained by the fact that the identification of fibers in these experiments was not sufficiently reliable.

If an equation for the cupula-endolymph-nerve system were quickly found, it would be natural to test whether the solution given by it corresponds with the experimental data obtained by rotation of the semicircular canal in its own plane with a constant angular acceleration α.

The differential equation in this case will have the form

$$\ddot{\theta} + \frac{c}{I}\dot{\theta} + \frac{k}{I}\theta = \alpha. \tag{25}$$

if with $t = 0$, $\dot{\theta} = 0$ and $\theta = 0$, then an approximate solution of this equation ($c/I >> k/I$) is:

$$\theta \approx \alpha \frac{I}{k}\left(1 - e^{-\frac{k}{c}t}\right). \tag{26}$$

Insofar as it follows from the conditions of supercritical damping that k/c is significantly less than unity, then the motion of the cupula defined by expression (26) will be very slow. Finally through an indefinitely long time interval ($t \to \infty$) the cupula will attain the maximum deflection /66

$$\theta_{\max} = \alpha \frac{I}{k}. \tag{27}$$

If as earlier we suppose that the change in impulsation frequency in the nerve is proportional to the deflection of the cupula, then with prolonged action of angular acceleration the frequency of rest discharge must increase slowly, asymptotically approaching the extreme value defined by the maximum deflection of the cupula (27).

Ledoux (1961), investigating the electrical activity of the ampullar nerve of a frog, showed that several seconds after the beginning of rotation of the preparation at a constant angular acceleration a change in impulsation frequency in the nerve deviated from the law predicted by (26); in addition a tendency for the frequency of discharge to return to the level of spontaneous activity was observed, despite the continuing action of angular acceleration. Analogously, if the semicircular canal is constricted so that a constant angular deflection is imparted to the cupula, after a short length of time the normal intensity of the changed electrical activity was restored.

This, while a natural experiment investigating the peripheral adaptation, possibly testifies to the fact that the pendulum theory with extended accelerated rotation of the canal is not generally applicable to the "cupula-endolymph-nerve" system.

But in nature animals are never subject to prolonged angular acceleration, inasmuch as all physiological motions are characterized by the fact that after short-term acceleration deceleration always follows, bringing the acquired velocity to zero. Therefore applying (26) to short time intervals τ, defined by the condition $\frac{k}{c}\tau \ll 1$, we obtain

$$\theta = \alpha\tau\frac{I}{c} = \gamma\frac{I}{c}, \tag{28}$$

Thus, for a small period of time τ, proceeding from the beginning of the action of constant angular acceleration, the deflection of the cupula is proportional to the instantaneous angular velocity γ, which is in complete correspondence with the change θ in oscillating motion, and also θ_{max} in the experiment with "stop stimulus".

In physiological movement the deflection of the cupula is always proportional to the instantaneous angular velocity, but not to the angular acceleration, although angular acceleration is an effective stimulus for the "cupula-endolymph" system. The integrating characteristic of the cupula-endolymph system is expressed by the equation /67

$$\theta = \frac{I}{c}\int_0^t \alpha dt. \tag{29}$$

For a physiological motion with an acceleration phase α_{acc} for a time period from 0 to τ_1 and a deceleration phase α_{decel} for a segment $\tau_1 - \tau_2$, after which a rest condition begins ($\theta = 0$ and $\dot{\theta} = 0$), (29) is expressed in the following way:

$$\theta = \frac{I}{c}\left(\int_0^{\tau_1}\alpha_{acc}\,dt + \int_{\tau_1}^{\tau_2}\alpha_{dec}\,dt\right) = 0. \tag{30}$$

In this case the deflection θ, introduced by the acceleration, is neutralized in the deceleration phase. After the completion of a physiological movement there is no residual deflection of the cupula (Groen, 1957).

Concluding the examination of electrophysiological investigations and the mathematical description of the function of the semicircular canals, it is necessary to note that the biological character of the object introduces the greatest complications into the simple pendulum model. Thus from the whole collection of ampullar nerve fibers only the proportional fibers precisely reflect the motion of the endolymph in the semicircular canals, since the remaining fibers give a distorted concept of it. But the characteristic curve of the entire nerve is significantly steeper than the curve of a single fiber, and consequently the sensitivity of the nerve is higher than the sensitivity of the fiber. Insofar as the curve has a rectilinear section, then, registering a change in frequency of discharge in the whole nerve with stop stimuli and sinusoidal oscillations of the semicircular canal, it is also possible to attain constants of the differential equation. But this equation will reflect the "viscous-elastic" characteristics of the cupula-endolymph-ampullar nerve system.

In single nerve fibers of the ampullar nerve of deaf mice, responses to sound tone stimulation and to stimulation by clicks were registered, directed to the semicircular canals with fenestration of the osseus labyrinth, the character of which is similar to the response of the auditory nerve (Mikaelin, 1964). All the fibers reacted to frequencies in bands from 80 to 4200 Hz, the lowest threshold for the appearance of the reaction being observed at 1500 Hz. A similar type of stimulation of the canals differs from the usual deflection of the cupula in one direction or another with physiological movements.

It is important to note that the reaction to sound stimulation was noted only in mice with a fenestrated labyrinth even a microphone response of the crista of the ampulla was recorded by many authors (cf. Chapter I). On the other hand, the investigations of /68
Jielof et al., (1952 and Kuiper (1956) on the lateral line organs of fish showed that removal of a large part of the cupula did not change the character of the microphone response, i.e., the perception of mechanical oscillation of acoustic frequency is a characteristic of the hair cells themselves. Thus, the hair cells of the labyrinth organs react both to static displacement and to the entire frequency spectrum of mechanical oscillation (Kuiper, 1956; Trincker, Partsch, 1959).

The adaptation phenomenon, which probably does not play such an essential role in physiological movement, could complicate the picture even more.

TABLE 4: REACTIONS WITH SIX SEMICIRCULAR CANALS TO ANGULAR DISPLACEMENT RELATIVE TO THE THREE AXIS (LOWENSTEIN, SAND, 1940b)

Semi-Circular Canal	Position Relative to the:					
	Longitudinal Axis		Transverse Axis		Vertical Axis	
	Right	Left	Right	Left	Right	Left
Front Right Vertical	Excitation	Inhibition	Excitation	Inhibition	Inhibition	Excitation
Left Front Vertical	Inhibition	Excitation	Excitation	Inhibition	Excitation	Inhibition
Right Rear Vertical	Excitation	Inhibition	Inhibition	Excitation	Excitation	Inhibition
Left Rear Vertical	Inhibition	Excitation	Inhibition	Excitation	Inhibition	Excitation
Right Horizontal	Reaction Absent	Reaction Absent	Reaction Absent	Reaction Absent	Excitation	Inhibition
Left Horizontal	Reaction Absent	Reaction Absent	Reaction Absent	Reaction Absent	Inhibition	Excitation

An electrophysiological investigation of the respones of all six semicircular canals with rotation around each of the three main spatial axes conducted by Lowenstein and Sand (1940) showed that the horizontal semicircular canal reacts only to rotation around the vertical axis, since the four vertical canals react only with excitation or with inhibition to rotation around any of the three primary spatial axes (Table 4). It must be emphasized that in all cases the frequencies of response of the canals were completely identical; the only exception might be in thresholds of responses, which were actually not analyzed. The table shows that the four vertical canals are functionally grouped in pairs with rotation around the three axes. So during rotation around the longitudinal /69 axis (deflections to the sides) they are laterally synergic; during rotation around the transverse axis (inclinations forward and back) they are transversly synergic, and during rotation around the vertical axis (rotation in the horizontal plane) they are diagonally synergic. The "privileged" position of the horizontal canals cannot be explained by simple mechanics. Probably this is associated with the fact that the vertical canals are in an earlier stage of evolution and have a planum semilunatum (Lowenstein, 1950).

There are also complications on a physical order. Thus, Vilstrup (1950), defining the horizontal semicircular canal of a

shark, observed that there was still a displacement of the cupula with rotation which could only be due to elasticity of the canal walls. On the other hand, Henriksson et al. (1966) introducing a fluid into the labyrinth of a frog, established a linear dependency between the amount of hydrostatic pressure in the labyrinth and the amount of fluid introduced. This dependency did not change essentially even when the liquid was drawn out or with a repeated introduction of fluid, which testifies to the elastic nature of the membranous labyrinth.

Thus the walls of the semicircular canal are elastic, are not hard and therefore have constituent endolymph velocities in a direction perpendicular to the axis of the canal (cf. Assumption 4).

Judging by the experiments of Kuiper (1956) and Flock (1965), the cupula of the lateral line organ of fish probably possesses not only elastic but also plastic characteristics, which in particular appear under the action of static force. Consequently Hook's law, used in the derivation of the equation, also has limited applicability (Assumption 1).

In 1956, S.G. Chebanov, observing the motion of a fluid in a glass model of the semicircular canal with an ampulla and utriculus under a microscope with a sudden stop,eliciting ampullopetal current in the fluid, found that immediately after stopping, a vortex arose first in the ampullar and two counter-vortices were formed in the utriculus. Thus if in the canal itself the motion of the fluid is laminar, in the ampullar and utricular portions it is vortical.

A large glass model of a semicircular canal with an ampulla, in which there was a densely fitted resinous cupula and a utriculus, Tonndorf and van Bergeijk (1958) showed that if the entrance and exit openings of the utriculus were located on one level then there were no differences in the deflection of the cupula with ampullopetal and ampullofugal fluid motion. The amount of deflection was linearly dependent upon the flow velocities with a spherical form of the ampulla and did not depend on the location of the alternating hydraulic resistance, provided that the overall resistance remained unchanged. If the entrance and exit openings were located at /70
different heights, a difference in the action of opposite currents on the cupula appeared; this difference was strengthened with a difference of heights.

When the size of the utriculus increased, the connection between the motive force and the deflection of the cupula became noticeably linear, at least with high flow velocities. In addition it was observed that the motion of the fluid through the utriculus, which was always laminar at low velocities, became vortical. This was probably related to a change in the Reynolds number due to the increase in the system's velocity during which the diameter of the channel underwent sharp changes. The presence of vortical motion

disturbs the Poiseuille law, which was used for the derivation of formula (18) and also the equation of motion (1). It is not clear whether a vortical motion takes place in the utriculus in a real labyrinth since the viscosity of endolymph can prevent the formation of utricular vortices with physiological motion.

Tonndorf and van Bergeijk (1958) also simulated the intra-utricular pressure, elevating the level of the fluid in the utriculus above the entrance and exit openings. It was found that the higher the pressure, the less the deflection of the cupula, given the same speed of the fluid in the canal. But Henriksson and Gleisner (1966), investigating the activity of the ampular nerve of a frog with experimental change of labyrinth pressure, showed that with the introduction of fluid into a labyrinth, the activity of the nerve increased and then returned to the original level before the introduction, and upon removal of the fluid (decrease in pressure) it decreased and did not return to the original level. Such changes could be associated with the system of introducing the fluid into the labyrinth. Probably upon introduction the cupula was deflected in the utriculopetal direction, and then with the establishment of a new level of pressure it returned to the rest condition under the action of its own elasticity. Upon removal of the fluid, the cupula probably was deflected in utriculofugal direction and then could not return to the rest position due to deformation of the ampulla.

Rotational vestibular responses with sinusoidal oscillations in the plane of the horizontal canal did not change with an increase in pressure in comparison with the norm. Probably divergences from the stimulated results of Tonndorf and van Berfeijk (1958) are explained by the elasticity of the canal wall. With a decrease of pressure the responses diminished and even disappeared. As was already noted, this was probably due to deformation of the ampulla.

Since with mechanical stimulation of the semicircular canal neither S. G. Chebanov (1956) nor Tonndorf and van Bergeijk (1958) were guided by the principles of dynamic similarity, then it is absolutely impossible to carry over the indicated results and all other results received by the authors to a real semicircular canal.

Miodrag (1966) observed the movement of fluid in a glass model /71 under a microscope which magnified 2x the sizes and shape of the human semicircular canals and showed that the variability of the cross section diameter has significance only with sudden stops of the rotational movement, with which along the semicircular canal in the utriculus the lowered pressure gradually transforms into an elevated pressure (with opposite directions of rotation the opposite occurs). It is interesting that along the same ampula the pressure remains the same with opposite directions of rotation, which agrees with the data of Tonndorf and van Bergeijk. This is very important since it leads to regular deflections of the cupula and protects the sensory epithelium from damage due to sudden changes in speed.

The Mechanics of the Otoliths and the Physiology of the Otolith Nerve

The differential equation assumed to describe the motion of an otolith (de Vries, 1950, 1956; Trincker, 1962) is analogous to the equation of motion of encolymph in the semicircular canals. If we consider the motion of the otolith only under the action of gravitational force, the equation will be recorded in the form

$$m_э\ddot{x} + c\dot{x} + kx = mg - \frac{m}{\rho}\cdot 1\cdot g, \tag{31}$$

or

$$\ddot{x} + 2\delta\dot{x} + \omega_0^2 x = \frac{\rho - 1}{\rho + 1} g \approx \frac{g}{2}, \tag{32}$$

where x, $\dot{x}$, $\ddot{x}$ are respectively the linear displacement, cm; the speed cm/sec and the acceleration, cm/sec^2 of the otolith relative to the sensory epithelium of the macula; c is the coefficient of friction forces, g/sec; k is the coefficient of elasticity forces, g/sec^2; $\delta = c/2m_{eff}$ is the damping coefficient, sec^{-1}; $\omega_0 = \sqrt{k/m_{eff}}$ is the circular frequency of the characteristic oscillation of the otolith, sec^{-1}; g the acceleration of the force of gravity, 981 cm/sec^2; ρ the density of the otolith, g/cm^3; m the mass of the otolith g; $m/\rho\cdot 1\cdot g$ the ejecting force acting on the otolith submerged in endolymph; m_{eff} the effective mass of the otolith, g, i.e., the summary mass of the otolith and the fluid displaced by its motion.

Assuming that the density of the endolymph is equal to the density of water and the displaced volume is equal to the volume of the otolith, we obtain an expression for the effective mass of the otolith in the form

$$m_e = m\left(1 + \frac{1}{\rho}\cdot 1\right). \tag{33}$$

For static displacement of the otolith ($\ddot{x} = \dot{x} = 0$) we have /72

$$\omega_0 x = \frac{g}{2}, \tag{34}$$

i.e., having measured the displacement of the otolith x, it is possible to define ω_0^2.

The maximum amplitude of displacement of the otolith under the action of a force changing according to a sinusoidal law with a frequency near ω_0 will be defined by the expression

$$x_{max} = \frac{a}{\omega_0 \delta}. \tag{35}$$

Here a is the maximum acceleration of the labyrinth with harmonic oscillation. Assigning an acceleration a, measuring the displace-

ment of the otolith x_{max} and knowing ω_0, it is possible to calculate the damping coefficient δ.

Having defined the weight of the otolith sacculus in experiments on more than 200 fish of 20 types, and according to roentgenograms, the displacement of the otolith under the action of gravitational force and the maximum amplitude of displacement (0.1 mm) under the action of a force changing according to a sinusoidal law, de Vries (1950) calculated the coefficients of the differential equation (31). It was found that the otolith sacculus of a ruff (Acerina cernua) is a harmonic oscillator with a critical damping ($\delta \approx \omega_0$).

It is interesting to note that if the return of the cupula of the semicircular canal from the deflected position to the position of equilibrium were characterized by the time constant c/k = 40 sec, then the indication time of the otolith characterized by the value $1/\delta$ is equal to 0.02 sec. de Vries could not precisely determine the coefficients c and k of the otolith utriculus, but assuming that the displacement is on the order of 0.005 mm and that the otolith utriculus is also critically damped, he obtained for the time constant the value 0.005 sec.

X-rays showed that the otolith sacculus was displaced only tangentially in relation to the epithelium, whereby even with centrifugal accelerations of 11 g displacement of the otolith comprises in all a total of 0.23 mm. The careful investigation by Vilstrup (1951b) demonstrated that during extreme changes of position of the head of a shark (Acanthias Vulgaris) only purely tangential displacement of the otolith utriculus in any direction on the order of 15 μm occurs.

Trincker (1962), investigating microphone response and change in potentials inside the layer of sensory cells of the macula caused by the motion of the otolith membrane in the utriculus of the guinea pig, showed that only a cutting force caused by the tangential shift of the membrane leads to bioelectric changes in potential. Forces located exactly perpendicular to the otolith membrane do not cause changes. Insofar as a cutting force is an effective stimulus for otolith receptors, changing with a change in position of the otolith relative to the direction of the force of gravity in sinusoidal law (Fig. 25), then it must be expected that the change in potential inside the layer of sensory cells and /73
a change in impulsation in the nerve innervating the macula otolith will also change according to sinusoidal law. Biologically this is very important since if pressure or expansion were an effective stimulus, then the stimulating force would change slowly with the increase in the angle of deflection, (i.e., as the cosine of the angle). The same cutting force increases sharply with small deviations from the normal position and more slowly with larger ones (Trincker, 1962).

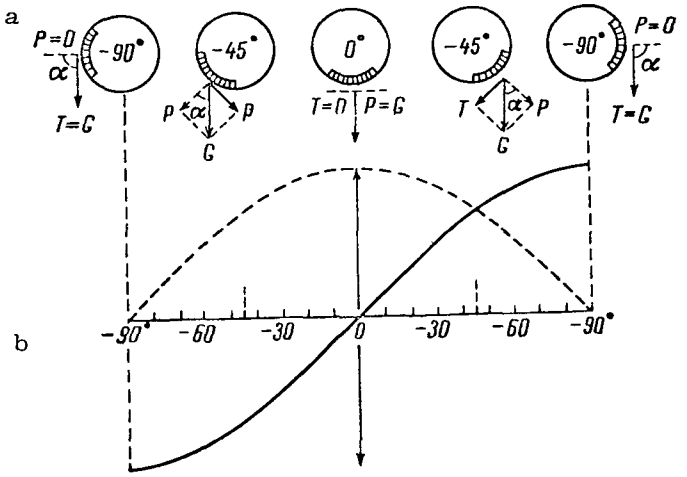

Fig. 25. Stimulation of the Macula Sensory Epithelium by a Cutting Force. (a) Systematic Depiction of the Utriculus with the Macula and the Otolith Membrane with Inclinations of the Head in a Frontal Plane; *G* - Force of Gravity; *T* - Cutting Force (Tangential Constituent); *P* - Pressure (Normal Constituent); (b) Connection of Cutting Force (Solid Line) and Pressure (Dotted Line) with an Angle of Deflection from the Vertical (Trincker, 1962).

The electrophysiological analysis of functions of various maculas, conducted on single fiber preparations of an isolated labyrinth of the thorny skate (Raja clavata) (Lowenstein, 1948, 1950, 1956; Lowenstein, Roberts, 1948, 1949, 1951), showed that in the labyrinth of the skate all three otolith organs (namely the utriculus, sacculus and lagena) take part in maintaining balance.

The sensory endings in the macula are usually characterized by a rest discharge, the frequency of which increases or decreases with a change in head position. The functional ranges of the utriculus and sacculus greatly overlap since both contain sensory endings reacting to lateral, forward and backward inclinations. /74
There are two main types of endings:some have a maximum of discharge activity in the "nose upward" position of the head (they predominate in the utriculus); others in the "nose downward" position (they predominate in the sacculus). Both types of functional units emit impulses also with a maximum frequency with the labyrinth upward, "head position", i.e., the same ending reacts both to lateral and to forward-backward inclinations. With slow rotation around the horizontal axis (transverse or longitudinal) a constant change in discharge frequency with activity maxima and minima in definite characteristic positions takes place. When a preparation is maintained in an inclined position, very weak adaptation is observed since the discharge frequency remains significantly higher or lower than the spontaneous frequency. With rotation in the opposite direction, the discharge frequency is produced entirely in reverse order. Thus the spatial position of the head for maximum

and minimum activity does not depend upon how the preparation was brought to the position. The described receptors give precise information on the position of the head in space at an absolute level of activity. The impulsation frequency increases very strongly with deflection at small angles, and in the majority of functional units the frequency changes present a clearly pronounced function similar to the characteristic curve of a cutting force (Fig. 25). Analogously, even the potential inside the layer of sensory cells changes (Trincker, 1962) whereby a shift of the membrane in one direction leads to depolarization of potential, and in the opposite direction to hyperpolarization.

There are also terminal organs, the activity maximum and minimum of which are diametrically opposed with opposite directions of rotation. They react to changes in head position by a decrease (increase) of activity, irrespective of the direction of change. After cessation of motion, the activity of these receptors quickly returns to the original level. Unlike the static position receptors, the receptors under consideration give information on the deflection from a definite position in space; they react to a constant speed of spatial deflections and they are called "out-of-position" receptors.

If we consider that between the principle position receptors and "out-of-position" receptors there are transitional types, and moreover the activity of the majority of receptors remains practically unchanged with a change in position, then it becomes apparent that the macula utriculus and sacculus are far from homogeneous structures. The diversities of receptors which react differently to inclination enables a more precise reflection by the sensory epithelium of mechanical displacement or of the otolith with a spatial change in head position. Receptors with constant impulsation, which remains even after removal of the otolith, probably have a tonic function(Lowenstein, 1956a).

Receptors in the lagena are also positional and react simultaneously to lateral and forward-backward inclinations, but are essentially different in their reactions from receptors of the utriculus and sacculus. As a rule they have a sharp maximum of activity near the normal position of the head, and therefore are called "into-level" receptors. /75

All the otolith organs reacted to linear accelerations in the plane of the macula.

Coppe and Ledoux (1951), experimenting on a preparation of an isolated labyrinth of a frog, registered spontaneous asymptotic discharges in the utricular nerve with any position of the head in space. The inclination of the preparation around any horizontal axis in one direction caused an increase in activity greater than with the opposite direction of inclination. Inhibitions of activity were never observed. An increase in the activity was especially intense during motion and somewhat weaker when the preparation was maintained in an inclined position.

Is not the participation of all 3 otolith organs of the skate excluded from perception of gravitational stimuli by reason of the function of these structures as vibration receptors?

Lowenstein and Roberts (1948, 1949, 1951) registered vibrational responses in the form of impulse discharges from nerve ramuli, proceeding from a portion of the macula sacculus, macula neglecta and lacinia utriculus of an isolated labyrinth of the skate (Raja clavata). Experiments showed the effectiveness of only vibrational stimuli, conducted to the preparation through the hard base on which it was located. Vibrations of the air did not elicit reactions.

Nerve fibers proceeding from the macula lagena did not react to vibrations. Even pure microphone responses were absent, although they were registered from all organs of the vestibular apparatus (cf. Chapter I).

Gravitational responses registered from the macula sacculus were basically limited to the rear third of the macula, whereby responses of the fibers innervating the most distant portion were purely gravitational and differed by the absence of microphone response. According to the amount of advance toward the front portion, there appear all the more pronounced microphone responses which are superimposed on the gravitational response. Finally, in 2/3 of the forward portion of the macula, purely vibrational responses are registered, which were not influenced by the spatial position of the preparation. The transition from one type of response to the other does not have a clear parallel in the structural characteristics of the macula and the otolith covering it, despite the fact that the rear portion of the otolith is more firmly connected to the wall of the sacculus than the forward portion. It is significant that within the bounds of one macula, covered by a massive unfragmented otolith, there are receptor mechanisms for the detection of changes in the direction of gravitational force and for the definition of phase shifts introduced by oscillations.

While in the sacculus, the macula is completely covered by the otolith, this is not observed in the utriculus. Here only the central portion, innervated by the main branch of the utricular nerve, is covered by the otolith. The same tongue-shaped extension of the macula on the roof of the utriculus process does not possess any covering structure. This unsupported portion of the utriculus is called the lacinia and is innervated by a separate nerve branch. The structual division of the macula utriculus into supported and unsupported portions has a functional significance. With the registration of action potentials from the main branch of the utricular nerve only gravitational responses are seen, and as a rule microphone effects are absent. Ramuli of the nerve innervating the lacinia do not detect responses to positional changes but are sensitive to vibrational stimulation. /76

Besides the receptors in the macula sacculus and the lacinia

utriculus, it was found that the macula neglecta (sometimes called the crista forta), not having an otolith covering but rather sensory hairs surrounded by a gelatinous secretion, is extremely sensitive to vibrations and does not react to inclinations and rotation. Vibrational responses of the macula neglecta differ from responses of the utriculus and sacculus by an extremely low threshold. The falling of a pin from a height equal to that of a man to a stone floor elicits a very clear reaction.

The greater portion of the sensory nerve endings indicates activity at rest in the absence of vibrational stimulation, but there are a significant number of silent sensory units. They are included in response with growth in the intensity of oscillation and indicate a significant range of thresholds.

In the experiments of Lowenstein and Roberts, vibrational responses to frequencies above 120 Hz were rarely registered, although the vestibular microphone response was observed up to a frequency of 750 Hz.

With a low intensity of stimulation, the frequency of spontaneous discharge decreased, With an increase in intensity, endings which were silent earlier are involved in the reaction and a significant synchronization of the frequency of response with the frequency of the stimulus takes place. This synchronization is very similar to that described for the cochlea of mammals, where it occurs at the lower limit of the acoustic spectrum.

The authors noted phenomena of adaptation to constant vibratory stimulation and a period of silence after the cessation of prolonged stimulation.

It is necessary to note that at first Ashcroft and Hallpike, who registered action potentials from the saccular nerve of a frog, found that rotation and inclination of the head did not produce any excitation and that this organ reacts to vibration up to a frequency of 512 Hz with impulse synchronization.

Ross (1935, 1936) also registered vibrational responses in /77
the anterior and posterior portions of the eighth nerve of a frog, but he did not precisely define the organs from which the responses arose.

Vibrational responses in utricular nerve of a frog were observed by Coppe and Ledoux (1951). Low frequency tuning fork vibrations elicited an increase in asynchronic activity in the nerve at median frequencies (500 Hz) and synchronic discharges of action potentials at the same frequency were observed. The authors registered microphone responses similar to the microphone response of the sacculus by conducting an electrode along the nerve to the utriculus .

The described experiments clearly showed that the otolith organs potentially possess a double function. They can serve as purely gravitational receptors with the function of connecting receptors of any linear accelerations (including centrifugal), or as vibration receptors, or simultaneously fulfill both functions (the sacculus of the thorn skate). The function of a given otolith organ is defined entirely by its structural characteristics, by its degree of support, and by its connections with auxiliary structures. In the labyrinth of elasmobranch fish all the potential possibilities exist simultaneously.

Cohen et al. (1953; 1955, 1958, 1960), registering activity of primary single nerve fibers in an isolated preparation of the statocyst of the lobster Homarus americanus, discovered a surprising functional similarity between the statocysts of invertebrates and the nonauditory labyrinth of vertebrate animals.

The majority of receptors of the statocysts in a lobster show activity in a state of rest. In the statocyst of the lobster, as in the utriculus of the skate, there are position receptors. Unlike the labyrinth position receptors, reacting simultaneously to inclinations relative to the longitudinal and transverse axis, the receptors of the statocysts react only to inclinations around the transverse axis. On the other hand, in the statocyst there are position receptors which react to absolute position of the head with inclination around the longitudinal (or transverse) axis, and at the same time manifest a clearly pronounced sensitivity to the direction of motion. In this type of receptor the characteristics of position receptors and out-of-position receptors are combined (or receptors of the semicircular canals). They signaled both the direction of motion and the absolute position, reached after cessation of motion. In the statocyst there are also acceleration receptors which react only to accelerated angular displacements around either spatial axis and do not react to absolute position. They are analogous to the receptors of the semicircular canals. /78
Although in invertebrate animals the semicircular canals are weakly sensitive to horizontal rotation and the horizontal canals react only to accelerated motions in their own plane (Lowenstein, Sand, 1940), the acceleration receptors of the statocysts are equally sensitive to angular displacement around any of the three main spation axis. Consequently the receptors of the semicircular canals give more precise information on the plane of angular displacement than the analogous receptors of a statocyst. In the statocyst of the lobster there are pure vibration receptors and also transition forms between the above enumerated types of receptors. Although arthropods have a smaller number of neurons than vertebrate animals, this insufficiency is compensated at least partially by the greater number of tasks performed by a single neuron.

Thus in the skate and the lobster, animals sufficiently far apart on the evolutionary ladder, information on position in the

field of gravitational force, velocity and direction of angular displacements enter the central nervous system in principally the same language; i.e., from the point of view of the peripheral coding of changes in the surroundings, the functional evolution is insignificant. The greater precision with which the higher animals integrate environmental changes is probably connected chiefly with the complexity of the central integration of efferent impulsation.

Much less definite results were obtained on mammals. Thus Wing (1963), registering neuron activity of the cells of scarpa's ganglion in a cat in response to stimulation of the otolith, did not discover any changes in activity in the majority of the cells. In the same reacting cells only responses which were delayed in time (up to 40 sec) and unsystematic were observed. The author even comes to the conclusion that in the cat the otolith organs of the utriculus and sacculus appear to be either rudimentary or, in general, do not participate in orientation of the animal in the gravitational field. Similar results may be explained by the elevation of thresholds of the neurons due to injuries caused by the operative approach to the ganglion and by the imposition of electrodes.

Sasaki et al. (1963) extracted the performance potentials from the utricular nerve of a rabbit with inclinations of the head and with linear accelerations, and found that the utriculus macula reacts to linear acceleration which is perpendicular to the plane of the macula, whereby stimulation of the otolith by pressure is seemingly more effective than by retraction. But it is true that a very small number of fibers were found which also react to cutting force. It is possible that this is connected with an incorrect spatial shape of the macula.

Under conditions of weightlessness, judging by the above- /79
described principals of the function of an isolated otolith preparation, the frequency of spontaneous nerve activity would hardly change, insofar as pressure on the macula is not an effective stimulus for receptor cells. In truth, if the otolith membrane has an incorrect shape or an inclined position in the cell in relation to the terrestrial vertical (so that at rest there is a constant tangential component of the gravitational force which is balanced by the elastic forces of the otolith membrane), then in a condition of weightlessness under the action of elastic forces the otolith membrane is somewhat displaced, which causes an increase in spontaneous activity (experiments of Copee, Ledoux, 1951).

On the other hand, due to the absence of pressure on the sensory epithelium and a decrease in the "friction" related to this during displacement of the otolith membrane along the sensory epithelium, a cutting force of a given quantity in weightlessness would produce a larger effect (increase in impulsation frequency) than under terrestrial conditions.

The activity of the nerve in weightlessness would remain constant with inclinations of the preparation, but linear acceleration and rotation would change the spontaneous impulsation. As a result, insofar as the tangential component of a resulting force vector acting upon the otolith is an effective stimulus, the natural difference between response on earth and under the condition of weightlessness (with all other conditions being equal) would be defined by difference in direction and magnitude of an equally acting and consequently tangential component due to the absence of weight of the otolith membrane.

Fiorica et al. (1962), registering the activity of scarpa ganglion of a cat during a free fall lasting 1-2 sec, noted an increase in general activity. Gualtierotti and Gerathewohl (1965), registering the activity of single nerve fibers of the utricular nerve of a frog (during parabolic flights where the condition of weightlessness lasted up to 30 sec) at the beginning of the condition of weightlessness, preceded by a period with a *G*-force of 3-4 units, noted a sudden increase in the frequency of spontaneous impulsation. At the time of weightlessness, the response to the horizontal acceleration differed by an impulsation frequency greater than that which would be obtained in a flight with a *G*-force of one unit. It is true, that blocking of response was observed after 10 sec., which was normalized after returning to a flight regime of 1 unit. The authors ascribed the appearance of blocking to inhibition maintained in time, caused by preliminary stimulation of the receptors during the period of high *G*-force, which preceded the condition of weightlessness. The increased response to linear horizontal acceleration, in the opinion of the authors, is partially due to this high *G*-force. Thus parabolic flight in an airplane does not give complete and precise information about the action of weightlessness on the otolith apparatus. An experiment on an isolated labyrinth, placed under conditions of an orbital flight, would help clarify this question.

The Semicircular Canals and the Otolith Organs

In first approximation the functional inter-relationship be- /80
tween the semicircular canals and the otolith organs is based on the fact that the semicircular canals react only to angular acceleration, while the otolith organs are sensitive to angular acceleration, to rotation at a constant velocity and to linear acceleration. But constant velocity of rotation is rarely found under natural conditions of animal life and therefore, positively, the majority of angular motions are related to the function of the semicircular canals.

There is no basis to assume that the semicircular canals react to linear acceleration on the order of magnitudes which an animal usually experiences. Therefore all of an animal's reflector responses to linear acceleration are controlled by the otolith organs. Inasmuch as under terrestrial conditions gravitational and all other

linear accelerations act simultaneously, the animal's reaction will be defined by the vectoral sum of forces acting upon the otolith. Thus centrifugal force, probably biologically important in bird flight, added vectorally to the force of gravitation will elicit a reflector response of a static nature.

Phylogenetically the interaction of the semicircular canals and the otolith organs could begin with the cyclostomata, where in the hagfish there is only one vertical canal with two ampullas and one otolith macula. The interaction between the very mobile cupula and the more inert otolith thus evidently appears very important, although potentially the otolith organ could register any motions and static inclinations (Lowenstein, 1956).

The Efferent System of the Vestibular Nerve

The first electrophysiological indication of the existence of an efferent system in the vestibular nerve could be considered to be the report of Ledoux (1958) on the fact that with calorization of a semicircular canal of the frog and the nerve of a similar contralateral canal, inhibition of commissure activity was observed.

In 1963, Schmidt undertook a special investigation of the efferent system of the vestibular nerve of a frog. He severed the ramuli of the vestibular nerve to all sections of the vestibular apparatus, with the exception of a ramulus to any one ampulla of the semicircular canal, and showed that accelerated rotation in the plane of this canal on the excitory side (and sometimes on the opposite) caused the appearance of impulse activity in the proximal ends of the severed ramuli of the contralateral labyrinth to all three ampullas to the utriculus, sacculus and lagena. Cutting /81 the remaining single ampulla ramulus in half, Schmidt registered commissure activity in the proximal portion of the severed ramulus during rotation. Complete section eliminated all activity in all ramuli of the vestibular nerves of both sides. It is natural that, leaving the vestibular nerve of one side intact, Schmidt discovered the occurrence of activity in all branches of the contralateral labyrinth, separated from receptors, during rapid rotation of the preparation around any spation axis. Slow rotation of the preparation (stimulation of the receptors of the otolith organs) did not produce any reaction in any one of the ramuli of the severed vestibular nerve. On this basis the author concluded that the efferent system does not react to stimulation of receptors of the otolith organs. Schmidt contributed the valuable observation that extralabyrinthal stimulations (pressing on the stomach or the eyes) elicited the appearance of commissure activity in any ramulus, but sound stimuli do not.

Thus Schmidt's investigations showed that the receptors of each ampulla are connected by efferent connections to all sections of the vestibular apparatus on both sides, and moreover there is a feedback loop from a given ampulla to itself.

Gleisner and Henriksson (1964), also in experiments on frogs, established that threshold accelerations for stimulation of the efferent system ($6°/sec^2$) were significantly higher than the threshold accelerations for the afferent system ($0.5°/sec^2$). The latency of the efferent system was not more than 200 msec and with small accelerations was significantly greater, even reaching several seconds, since the latent period in the afferent system was absent (a limit of precision of measurements of the authors was 100 m/sec). The efferent response was characterized by great variability of thresholds and also of impulsation frequencies, so that the clear connection between stimulus (acceleration increased in time) and response (frequency of stimulation) established by Groen et al. (1952) and examined by us above probably was not sufficient for activity in the efferent system. The authors also noted that ether had a blocking effect on efferent activity. Bertrand and Veenhoof (1964) showed on rabbits that impulses in the proximal section of a severed vestibular nerve arise with the stimulation of the otolith receptors on rockers. Probably efference of the otolith organs also have high thresholds, and precisely for that reason Schmidt (1963) did not discover any reactions of the efferent system to slow inclinations.

Sala (1963, 1965) performed experiments on cats in the aim of demonstrating the changes to afferent vestibular activity elicited by stimulation of the efferent vestibular system. Afferent activity was registered both in the vestibular nerve (first series of experiments) and in the vestibular receptors (second series of experiments). Thus the activity of the efferent nerve system on action potentials /82 of the vestibular nerve and on the condition of excitability of the same vestibular receptors was investigated. In the first series of experiments, the author investigated changes in impulse activity in the vestibular nerve with stimulation by rectangular electrical stimuli of the region of contralateral vestibular nuclei (duration of stimulus 0.1 to 1 msec, amount 0.5 - 4 G). The results of this series of experiments showed that only electrical stimulation of the region of Deiter's contralateral nucleus caused a change in afferent activity of the vestibular nerve. A single stimulation always caused the appearance of afferent activity and tetanic stimulation, exerting an inhibitory action on the spontaneous action potentials of the vestibular nerve and on an increased impulsation frequency caused by galvanic polarization of the labyrinth. The author assumes that changes in activity of the vestibular nerve in these experiments are explained by stimulation of the efferent vestibular system and considers three basic objections to such an interpretation of the obtained results. In the first place, it is possible that impulses registered in the vestibular nerve are only antidromic discharges, conducted along the vestibular nerve due to stimulation in the region of the contralateral vestibular nuclei. This is excluded due to the extended latent period (20-30 msec) between stimulation and the appearance of action potentials in the nerve. Moreover the original vestibular fibers do not intersect the middle line (Walberg et al., 1958; Shimazu, Precht, 1966) thereby also excluding the possibility that impulses conducted from the vestibular nerve were

produced by the vestibular neurons of the second order, i.e., the observed phenomenon is connected with the internucleic effect.

In the second place, changes in bioelectric activity can be caused not by the stimulation of the efferent system, but by diffuse propagation of an electrical stimulus to the vestibular receptors through the tissue of the fourth ventricle. Such a possibility is also excluded due to the prolonged latency of the response, the moderate intensity of stimuli, the small size of the stimulated region, and also the facts that the effect disappears after shallow section of the brain stem along the middle line and that only the stimulation of specific places on the surface of the bottom of the fourth ventricle produces the described changes.

In the third place, electrical activity possibly was conducted not only from the axon, but also from the cellular bodies scattered along the original fibers of the vestibular nerve. In this case the observed phenomena could be due to interneuron influences on the vestibular fibers of the second order. But, in the opinion of the author, even this is impossible since cellular bodies distributed along the vestibular nerve functionally belong to g. scarpa, i.e., they appear as primary afferents (Brodal et al., 1966).

Thus, the observed phenomenon can be explained if we assume /83 that the stimulation of the bottom of the fourth ventricle causes activation of the efferent system, direct or indirect, through stimulation of the nerve structure, anatomically closely connected with the efferent vestibular system.

In the second series of experiments with caloric stimulation by water through an ear holder (warm water 50° and cold water 5°; 30 cm^3, irrigation for 30 sec) a change in constant potential was discovered both on the stimulated side (which indicates that the labyrinth was unharmed) and on the contralateral side. With stimulation by warm water in the ipsilateral labyrinth, depolarization arose; with stimulation by means of cold water, hyperpolarization. Maximum changes in potential totalled 300 μV.

Electric stimulation of the efferent vestibular system (ipsilateral and contralateral regions of Deiter's nuclei and at the level of the suture of the rhomboid fossa,) caused an increase in the rest potential; i.e., hyperpolarization. The latency of the effect equalled 9-12 msec. Such a latency excludes the possibility of antidromic activation of the nerves. The maximum effect developed in 50-100 msec and fluctuated within the limits of 100-200 μV. The amount of change depended on the intensity of the stimulation. After cessation of stimulation, the constant potential returned to the original level in 75-90 msec.

A curious picture was observed with tetanic stimulation of the contralateral Deiter's nucleus. The optimal frequency of stimulation was 150-300 imp/sec, duration of the impulse 0.5 msec), amount

2-6 V; stimulation was produced several times per minute, extent of stimulation 20 msec; intervals between stimulations 150 msec. In this case each impulse caused hyperpolarization of the sensory epithelium. After cessation of stimulation, depolarization was observed for a short period of time. These phenomena were especially pronounced with stimulation of the region of the contralateral Deiter's nucleus. With stimulation of equal intensity to the region of the ipsilateral nucleus and the region of the suture such a phenomenon was observed but of less intensity.

Electrical stimulation of the efferent vestibular system increased hyperpolarization, caused by cold caloric stimulation, and decreased depolarization caused by a warm thermic stimulation.

Intravenous introduction of strychnine in a dose of 0.1 mg/kg caused, in animals, a decrease of changes in constant potentials of the sensory epithelium (up to full suppression) developing due /84
to the electric stimulation of Deiter's nucleus. Weakening or blocking the effect of efferent stimulation with intravenous introduction of strychnine confirmed its antagonizing action as an inhibitor of post-synaptic potentials of motoneurons in the spinal cord (Eccles et al., 1954), and of centrifugal inhibition, conducted along Rasmusen's olive-cochlear fibers (Desmedt, Delwaide, 1963).

Changes in the constant potential of the labyrinth after cold or warm caloric stimulation agrees with the observations of Trincker (1959), who showed that in the horizontal semicircular canal the utriculopetal and utriculofugal deflections of the cupula caused, respectively, de- and hyperpolarization of the constant potentials. Lowenstein (1955), Trincker (1959), Dohlman (1960) and Eldredge et al. (1961) emphasized the importance of these labyrinth potential constants as generator potentials of the afferent activity of the vestibular nerve. Changes in afferent activity take place due to the phenomenon of depolarization (strengthening spontaneous activity) and hyperpolarization (decrease or disappearance of spontaneous activity in the sensory neuroepithelium). The fact that thermic (warm and cold) stimulation of the labyrinth causes simultaneous changes of the opposite sign in the contralateral labyrinth can be considered only as evidence of existence of the efferent vestibular system.

Insofar as experiments were completed on animals with precollicular decerebration, and in several cases even with removal of the cerebellum, then it is possible to assume that activation of the efferent vestibular system by afferent impulses of a stimulated labyrinth exist through intercalary neurons of the ponto-bulbar reticular formation.

Even in the second series of experiments, the prolonged latent period (9-12 msec) excludes the possibility of antidromic conduction of electrical impulses. On the other hand, insofar as registration was accomplished at the level of vestibular receptors then a change

in their activity can be explained only by the direct action of the efferent fibers on the sensory neuron epithelium with which they are in direct contact.

Preliminary results of Sala's interesting investigation allow us to draw several conclusions about the functional significance of the efferent system. Undoubtedly the activity of the efferent vestibular system is manifested primarily in inhibitory action on the afferent activity of the main vestibular neurons, whereby this action develops at the level of the neuroepithelium of the ampullar receptors. This inhibitory action is especially clearly seen at the time of tetanic stimulation of the efferent vestibular system. But several results obtained by Sala lead to the conclusion that actually the activity of the efferent system is more complex. The /85 author observed that electrical stimulation of the efferent vestibular system by single impulses causes the appearance of afferent activity in the vestibular nerve, which is an expression of excitation of the vestibular receptors. This effect may be explained, having assumed that the activity of the efferent vestibular system leads to an inhibitory effect, but is not discovered in the vestibular nerve due to the subsequent output effect. This hypothesis is strengthened by the fact that the latent period between a single stimulus and the vestibular afferent commissures is definitely longer (22-32 msec) than the latency between stimulation of the efferent vestibular system and the appearance of hyperpolarization of the ampullar receptors (9-12 msec). Further tetantic stimulation of the efferent vestibular system causes the appearance of hyperpolarization of the receptors which is accompanied, after cessation of the stimulus, by a drop in potential to below the original level; i.e., depolarization. Consequently the function of this system is more complicated than simple inhibition. This assertion is strengthed by the fact that warm stimulation of a labyrinth showed an influence on the constant potentials of both labyrinths. In addition, it was noted that cold stimulation hyperpolarizes and warm stimulation depolarizes potentials of the ipsilateral labyrinth, simultaneously depolarizing or hyperpolarizing the contralateral labyrinth.

Thus stimulation of one labyrinth causes opposite changes in potential in each labyrinth. This fact acquires special significance if we consider that similar phenomena probably take place under physiological conditions . Actually, utriculopetal deflection of the cupula, in the case of the horizontal canal, leading to a depolarization of potential of the sensory epithelium and to an increase in the frequency of spontaneous activity in the ampullar nerve, is always accompanied by utriculofugal deflection of the cupula in the opposite canal, and correspondingly by hyperpolarization, a decrease and even the disappearance of activity in the ampullar nerve. Such reciprocal changes in the peripheral regions play an important role in the functional mechanism of the two vestibular apparatus (cf. Chap. III). It is possible to assume that even the efferent system in turn must exert a modulating in-

hibitory or excitory action on the efferent activity in correspondence with the functional condition of the receptors.

The investigations of Sala, and in particular the results obtained with thermic stimulation and simultaneous registration of potentials of both labyrinths, showed that there is a feedback loop between both labyrinths (Fig. 26). This feedback must arise on the /86
ponto-bulbar level, according to the following model: labyrinth receptors of one side--primary afferent vestibular neurons--vestibular nuclei and reticular formation--cells of the efferent vestibular system--efferent vestibular fibers--ipsilateral and contralateral labyrinth receptors. The physiological importance of the efferent

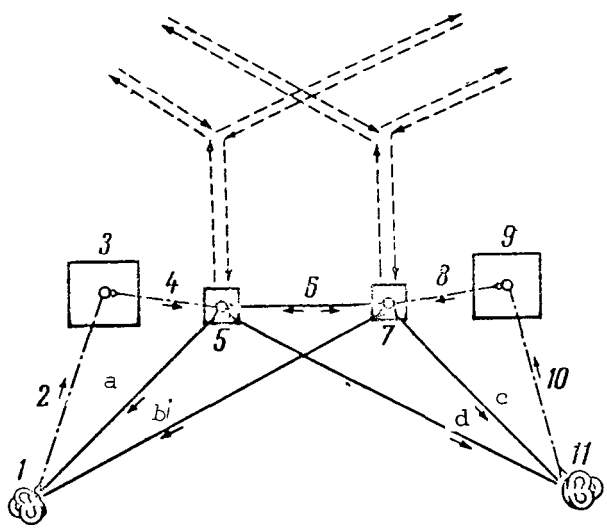

Fig. 26. Schematic Drawing of the Efferent Vestibular System. Solid Line: Fibers of the Efferent System of the Vestibular Nerve. Dashed Line: Afferent System of the Vestibular Nerve. Dotted Line: Polysynaptic Connections of the Efferent Vestibular System with Higher Centers. (1) Ipsilateral Labyrinth Receptors; (2) Primary Afferent Vestibular Fibers; (3) Ipsilateral Vestibular Nuclei; (4) Connection of the Ipsilateral Vestibular Nuclei with an Ipsilateral Cell Group of the Efferent Vestibular System; (5) Cellular Group of the Efferent Vestibular System; (6) Connection of the Ipsilateral and Contralateral Efferent System Through Unknown Intermediate Neurons or Specific Efferent Fibers; (7) Contralateral Cellular Group of the Efferent Vestibular System; (8) Connection of the Contralateral Vestibular Nuclei with the Contralateral Group of Cells of the Efferent Vestibular System; (9) Contralateral Vestibular Nuclei; (10) Primary Afferent Vestibular Fiber; (11) Contralateral Labyrinth Receptors; (a) and (b) Ipsilateral Efferent Fibers; (c) and (d) Contralateral Efferent Fibers (Sala, 1965).

vestibular system appears more ovbious if we remember that each labyrinth consists of three semicircular canals having close functional synergism with one another and with a canal on the opposite side (cf. Table 4). Sala (1965) assumes that future experiments /87
will probably show that the higher nervous centers are found in close anatomical and general physiological connections with the peripheral afferent vestibular system, as was shown for other efferent systems. This connection can exist through nonspecific activity at the level of the reticular formation of the brain stem and specific activity conducted anatomically by definite centers and fibers.

For the vestibular function the central control of activity is especially important since the vestibular apparatus with its numerous receptors, under constant stimulation by gravitational and kinematic stimuli participates in the regulation of muscle tone and play a basic role in the maintenance of static and dynamic balance.

The hair cells of the vestibular epithelium are sensory cells which are innervated by branches of nerve fibers going to the central nervous system. Numerous nerve endings are in contact with each hair cell; among them both afferent and efferent nerve endings are identified. On an afferent nerve ending, the synaptic transmission begins in the region which shows specialized ultrastructural organization, characterized by the presence of synaptic patches and vesicles. A resemblance between these vesicles and synaptic vesicles attests to the neuro-humeral synaptic transmission to the afferent nerve ending. Each afferent nerve fiber is in contact with several hair cells. Such an arrangement can essentially lower the threshold for the appearance of action potentials due to the spatial summation of subliminal stimuli.

Afferent nerve fibers carry sensory information to the central nervous system with the aid of frequency modulation of spontaneous activity. Displacement of the cupula (otolith membrane) in the direction which causes depolarization of the sensory nerve fibers is excitary and leads to an increase in the discharge frequency, while displacement in the opposite direction leads to depolarization, is inhibitory, and is accompanied by a decrease in the discharge frequency. Sensory information presented by the receptor potential is then reflected by the frequency of action potentials, transmitted into the central nervous system by afferent nerve fibers. The amount of deflection of the cupula from the normal position is indicated by the frequency of afferent impulses. The precise connection between frequency of afferent impulses and receptor potential with vibrational and static displacement of the cupula (otolith membrane), and also the shift in potential accompanying microphone response, still remains to be investigated.

Efferent nerve endings innervating the hair cells probably /88
represent a feedback system, capable of changing peripheral sensory response.

Morphological investigations into structures of the semicircular canals in otolith organs perceiving adequate stimuli indicated that they have, principally, a similar structure: a base formed by supportive and sensory hair cells (crista in the semicircular canals, macula in the otolith membranes), and an intermediate layer (subcupular or submembranal space) which allows the possibility for a mobile structure (cupula or otolith membrane), with the action of acceleration on the inertial mass (angular accelerations on the mass of the endolymph in the semicircular canals and linear accelerations on the mass of the otolith membranes), to move relative to the sensory epithelium.

The mobile structure is an instrument transforming the partial form of mechanical motion into a stimulus of sensory cells. Such a stimulus is a cutting displacement of the mobile structure along the sensory epithelium.

In the first approximation the characteristics of the mobile structures with the action of adequate stimuli are described by linear equations of the second magnitude with constant coefficients.

The nerve innervating the receptors of the crista of the semicircular canal consists of one type of afferent fiber reacting, in the case of a horizontal canal, with an increase in impulsation frequency upon the displacement of the cupula toward the utriculus and with a decrease (if there is spontaneous activity) with opposite displacement. In the vertical canals, changes in activity bear the opposite character. This is the only type of fiber which is separated into two subgroups; spontaneously active fibers with a low threshold, and high threshold fibers which are silent at rest. Differences in the functional characteristics of silent and spontaneously active units are probably connected with the number and condition of synapses in the sensory cell. Less sensitive silent units, then, would correspond to the sensory cell with a smaller number of functional synapses.

The uniformity of the characteristics of separate fibers, and consequently of the whole trunk of the ampullar nerve, corresponds well with the homogeneous morphological polarization of the sensory epithelium of the crista. Kinocilia of all sensory cells are located along one side of the hair bundles. In the cristae of horizontal canals, the kinocilia are always located on the utricular pole of the cell surface; in cristae of the vertical canals they are on the canal pole. Consequently reverse functional characteristics of the cristae of the horizontal and vertical canals are connected with the reverse morphological polarization of sensory hairs.

The otolith nerve consists of uniformly reacting afferent fibers, which correlates with the complex polarization of hair bundles of /89
the sensory cells and with the various types of bundle organization. In the macula utriculus the direction of polarization flabellately

diverges from the internal edge to a certain line behind which the direction of polarization is the opposite. Kinocilia on various sides of this arbitrary line are directed against each other. Thus all possible directions of polarization are present in one macula utriculus.

If we assume that there is the same mechanism of stimulation of cells in the macula as in the crista, positive stimulation with increase of impulse activity will rise when sensory hairs are deflected towards the kinocilia. Insofar as in the maculu utriculus all directions of polarization are represented, one macula is capable of reacting to rectilinear acceleration in all directions.

In the macula sacculus, all directions of polarization are not present. The sensory cells are approximately polarized equally in the forward lower and rear upper directions, whereby along both sides of the line dividing these directions of polarization, the kinocilia of bundles are turned in opposite directions.

Changes in frequency in the ampullar and otolith nerves within definite value limits of adequate stimulation quite precisely reflect the motion of mobile structures. However in intact animals, due to the existence of efferent feedback systems, characteristically afferent systems could never be described by differential equations of the second magnitude with constant coefficients, since coefficients of such an equation would depend upon efferent control.

CHAPTER III

THE VESTIBULAR NUCLEI

Brief Information on the Anatomy and Cytoarchitectonics of the Vestibular Nuclei

The majority of authors separate four principal nuclei in the /90
vestibular complex: the superior, lateral, medial, and descending (inferior). Inside each of them there are regions which primary vestibular fibers do not enter. A. Brodal et al. (1966) consider that for purely practical reasons it is useful to preserve the existing nomenclature, especially since "vestibular" and "nonvestibular" portions of various nuclei display common features in relation to connections and architectonics. Corresponding with this point of view, several smaller topographically closely cellular groups connected with the four basic vestibular nuclei are included by these authors in the vestibular complex, even though they are not fed by primary vestibular fibers.

The complex of vestibular nuclei extends in the oro-caudal direction at a distance of 9.2 to 12 mm. The medial nucleus is distinguished by the greatest extension.

TABLE 5

EXTENSION OF VESTIBULAR NUCLEI IN MAN (in mm)

Nucleus	According to Olszewski and Baxter (1954)	According to Ponomarev (1958)
Medial	9	6.6(5.0-8.3)
Lateral	4	4(2.9-5.8)
Superior	4	4.4(3.4-5.4)
Descending	5	2.8(2.0-3.8)

Blinkov and Ponomarev (1965) made a quantitative determination /91
of the neurons and glial cells in the vestibular nuclei of man, monkeys and dogs. The total number of neurons in the nuclei of one

half the brain in man is 245,000, in the monkey 143,000 and in the dog 134,000.

TABLE 6

QUANTITATIVE DETERMINATION OF NEURONS AND GLIAL ELEMENTS IN VARIOUS VESTIBULAR NUCLEI IN MAN, MONKEYS AND DOGS. (Blinkov, Ponomarev, 1965)

Object of Investigation	Nucleus			
	Medial	Descending	Lateral	Superior
	Number of Neurons per Nucleus (in thousands)			
Man	117.4±6.7*	46.9±2.3	47.0±4.6	33.4±4.5
Monkey	76.9±5.8	33.7±4.0	15.7±7.9	16.8±6.5
Dog	64.3±8.1	28.5±0.5	17.9±1.4	23.5±4.4
	No. of Neurons per 0.001 mm^3			
Man	5.6±0.9	5.0±0.5	3.1±0.5	2.3±1.0
Monkey	11.5±0.7	7.2±0.6	2.7±0.5	6.3±0.9
Dog	8.4±1.3	4.0±1.5	1.9±0.4	4.6±0.5
	No. of Glial Cells per 0.001 mm^3			
Man	125.3±9.3	136.2±8.7	137.3±5.8	113.6±15.8
Monkey	140±21.3	145.3±7.8	144.6±12.7	135.3±16.7
Dog	186.6±11.7	162.3±32.1	156.8±39.8	162.6±31.1

*Mean ± Standard Deviation

It is apparent from this table that the number of neurons in each nucleus in man is greater than in monkeys and dogs.

With the exception of the lateral nucleus, the correlation of nucleic density in the monkey and dog are approximately the same as in man.

In the lateral nucleus of the monkey and the dog, the neuron density is less than in the superior nucleus.

Internal Organization of the Vestibular Nuclei

G. P. Zhukova (1965) studying the morphology of the vestibular nuclei by Golgi's method in cats, dogs and rats, comes to the conclusion that the various types of nucleic cells can be classified in three groups: specific, nonspecific and transitional. Such a structure is inherent for all nuclei of the brain stem. Thus in the brain stem the neurons of well-differentiated specific formations (entering in the composition of analyzers and motor nuclei

systems) and neurons typical of the reticular formation are clearly differentiated according to basic indicators of structure: the first are characterized by thick, branching and twisting dendrites, short in the sensory and long in the motor formations; the second have few, little-branching dendrites and long dendrites (Zhukova and Lentovich, 1964; Zhukova, 1965). These two neuron shapes, as the authors assume, are basic in all sections of the central nervous system. But in its caudal sections, i.e. in the brain stem and in the spinal cord, there is a significant number of neurons, transitional in structure, between the typical specific and typical reticular types. Such elements are found either in the region of the reticular formation or inside specific formations. In the latter case transitional neurons, together with typical reticular neurons also penetrating the given formations, compose the reticular components as well as the inherently specific component. G. P. Zhukova (1965) considers the correlation of the indicated neuron groups (specific, reticular and transitional) on cross sections of three different levels. The first level corresponds approximately to the center of the caudal-rostral portion of the descending and medial nuclei; the second passes through the rostral end of the descending and medial nuclei through the lateral nucleus (Deiter's) and the interstitial nucleus; and finally the third intersects only the superior nucleus (Bechterev's). /92

On the first level the following characteristics of the neuron structure are present. The medial nucleus is represented by typical reticular neurons and, to a lesser degree, by neurons of transitional shape. Transitional neurons differ from reticular ones by the large amount of branching and the thickness of dendrites which gives them the well-known resemblance to specific cells (Fig. 27).

In the medial nucleus, the transitional neurons are more similar to reticular ones than to specific elements and are frequently found in the lateral portion of the nucleus. Typical reticular neurons are especially characteristic for the medial portion of the nucleus, which without a visible border passes into the reticular formation of the medulla oblongata. In the medial nucleus there are no typical specific neurons. The nucleus under consideration passes into the descending nucleus in a lateral direction.

A large part of the descending nucleus also consists of neurons of the reticular or transitional types. However, here the transitional neurons predominate, some of which acquire a significant resemblance to specific types. Moreover, unlike the medial nucleus, the descending nucleus has typical specific neurons, scattered primarily in its lateral portions. Thus the neuron structure of these two nuclei changes in a medial-lateral direction in a definite way: in the medial portions, the reticular types predominate; in the intermedial, transitional; and in the lateral, specific neurons.

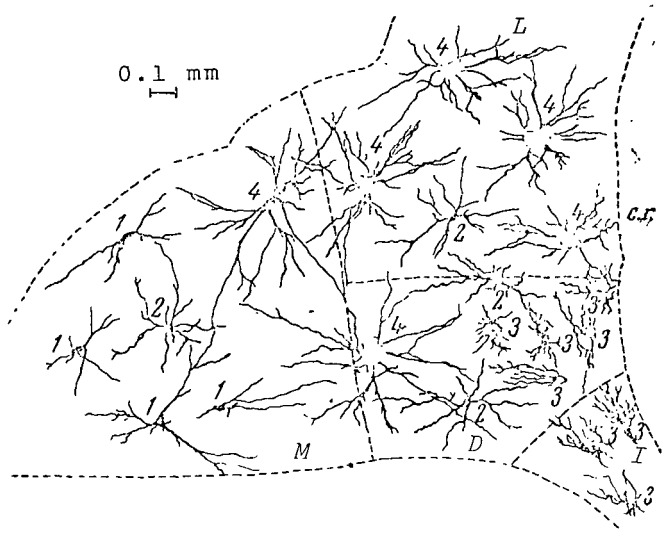

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Fig. 27. Chart of Neuron Structure of the Rostral Level of the Medial (*M*), Descending (*D*), Interstitial (*I*), and Lateral (*L*) Nuclei.

1. Reticular Neurons; 2. Neurons of Transitional Form; 3. Neurons of the Specific Type; c.r.=restiform Body (Zhukova, 1965).

Consequently, as the author indicates, a gradual transition of reticular neurons into specific ones through a series of intermediate neurons is observed.

On a more rostral level, the neuron characteristic somewhat changes, which is caused by the appearance here of a gigantocellular lateral nucleus (Fig. 27). The gigantic cells of this nucleus can be related to the same type of neurons as the gigantic cells of the reticular formation. According to the way they are structured, they represent transitional elements, from reticular to specific, but differ by their gigantic or large sizes. These transitional neurons are more similar to specific cells than to reticular types. Their resemblance to motor neurons of the spinal cord is especially pronounced. Gigantic or large cells of transitional form penetrate the adjacent portions of the medial and descending nuclei (*M*4, *D*4). This especially pertains to the medial nucleus, which in the rostral section neighbors the lateral nucleus for a great distance, while the descending nucleus, with the appearance of the lateral nucleus, swiftly tapers down to nothing. On the other hand,

the small transitional neurons characteristic of the medial and descending nuclei are found in the portions of the lateral nucleus adjacent to the nuclei (*L*2). However, at the given level the interpenetration of structures of various nuclei is expressed to a lesser degree than on the underlying level. At this level cells of the specific type are distributed with greater concentration (*D*3); here they are more numerous, since they are found not only in the descending but also in the interstitial nucleus. They are concentrated in the most lateral portion of the descending nucleus and in the interstitial nucleus touching it on the lateral side, which basically consists of new cells.

At the level under consideration the same order of distribution of various neuron forms is basically preserved, just as it is in a more caudal direction. Specifically reticular neurons predominate in the medial, and specific neurons in the lateral sections of the entire complex of nuclei, while neurons of transitional types, including gigantic neurons, basically occupy an intermediate position (Fig. 27). This is clearly seen in the ventral section where medial, descending and interstitial nuclei are present. However, as opposed to the preceding level, here there are more transitional and specific neurons than typical reticular neurons. Thus a significant decrease in the number of typical reticular neurons is noted the more one passes in a rostral direction, and an increase in the number of specific or neurons approximating them in structure is also noted. /94

On the most rostral level is the superior vestibular nucleus, which basically consists of typically specific neurons (Fig. 28). These neurons comprise the greater central portion of the nucleus and are distributed more compactly than cells of the underlying nuclei. Due to the indicated structural characteristics, the superior nucleus is sufficiently clearly separated from the other nuclei of the vestibular complex. However, there are single neurons of the reticular transitional type in it which are found primarily in the peripheral regions of the nucleus or in a small number between the specific cells, dividing these latter into islets.

The differences in neuron structure of the vestibular nuclei described above correspond in their basic features with the generally accepted classification of these nuclei developed on the basis of the cytoarchitectonic method. However the study of neuron structure by Golgi's method showed that the vestibular nuclei are separated from one another unequally clearly in the rostral and caudal level. Thus at the level of the medial and descending nuclei, where it is possible to observe only a gradual transition from the reticular neurons to specific neurons, it was not possible to establish a precise boundary between the two nuclei. On a more rostral level, a group of specific cells of the interstitial nucleus is distinguished which, however, adjoins the similar cells of the

adjacent portion of the descending nucleus. Here even the lateral nucleus, constructed of cells which are close to specific cells, /95
is noticeably different from other structures. Finally, the most rostral superior nucleus, consisting basically of specific cells, is a completely separate formation. Aside from the caudal to the rostral pole of the complex of vestibular nuclei, the quantitative relationship of various neuron forms changes. At the caudal levels, reticular cells, or cells similar to reticular cells, predominate. At more rostral levels, the number of specific cells or cells approximating specific cells increases. At the most rostral level these typical specific cells compose the basic mass of elements.

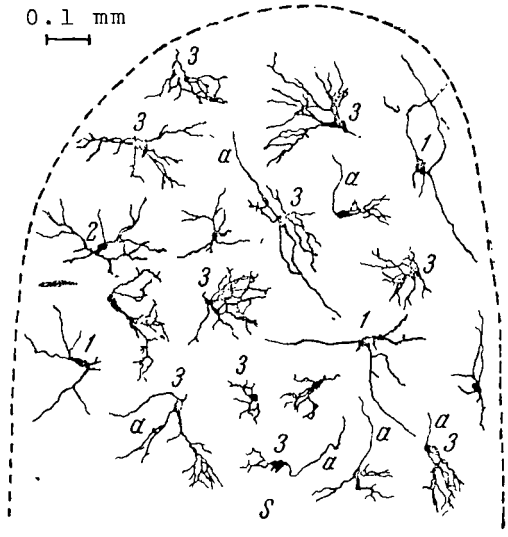

Fig. 28. Chart of the Neuron Structure of the Superior Nucleus. The Same Types of Cells are Designated with Numbers as on Fig. 27. *a* = axon. (Zhukova, 1965).

Thus on the basis of characteristics of the neuron structure of the vestibular nuclei, it is possible to judge their ever increasing structural differentiation in the caudal-rostral direction. Moreover, the study of neuron structure permits us to note the definite character of their changes even in the medial-lateral direction; reticular cells, numerous in the medial portions of the nucleic complex, are replaced by transitional and finally by specific forms of neurons in its lateral portions. These correlations are clearly noted on the mean central level of the vestibular nuclei. The medial nucleus, especially its caudal and medial portions which are directly fused with the reticular formation, displays reticular structural features to the greatest degree. Only the superior and interstitial nuclei in the /96
vestibular complex appear as classical specific formations.

Are there fibers from various portions of the labyrinth distributed in definite zones of the vestibular complex? The only studies on this question are the reports of Lorento de No (1926, 1933), who described in detail the bundles coming from the separate cristae and maculae, defined the topography of the cells in the vestibular ganglion and made a careful analysis of the distribution, inside the vestibular nuclei, of the fibers originating from various portions of the vestibular ganglia (investigation was carried out on mice by Golgi's method). These fibers can be divided into

5 groups. The fibers in the cristae of the semicircular canals (Groups I and II) end in the superior nucleus in the most lateral portion of the descending nucleus, and partially in the medial nucleus. These fibers do not feed Deiter's nucleus, the ventral portion of which receives vestibular afferents from the utriculus macula (Group IV). Group IV fibers do not arrive at the superior nucleus or, apparently, at the medial nucleus; at the same time some of them, evidently, end in the descending nucleus fibers from the sacculus macula (Group IV), probably, pass basically to the dorsal lateral portion of the descending vestibular nucleus. Thus, it is found that the superior nucleus is fed only by fibers from the cristae of the semicircular canals. The question of whether the lateral nucleus is fed only by utricular fibers remains open; thus it is impossible to establish definitely whether the utriculus or cristae is the exact origin of Group II or III fibers which end in Deiter's nucleus, and supposedly also in the medial nucleus.

After the studies of Lorento de No, it became evident that although fibers from the maculae and the semicircular canals have, in part, different central representation, as a rule the distribution of afferents from various receptor regions of the labyrinth in specific portions of the complex of the vestibular nuclei still is not selective.

A simplified and systematized depiction of the basic afferent and efferent connections of the vestibular nuclei is presented in the schematic drawing (Fig. 29) borrowed from A. Brodal and others (1966).

The superior and lateral nuclei, morphologically more clearly differentiated, connected with thicker peripheral afferent fibers and originating magistral efferent paths, probably are specialized for the perception and the rapid directional transition of epicritical vestibular sensitivity in an ascending (through the superior nucleus) or descending (through the lateral nucleus) direction.

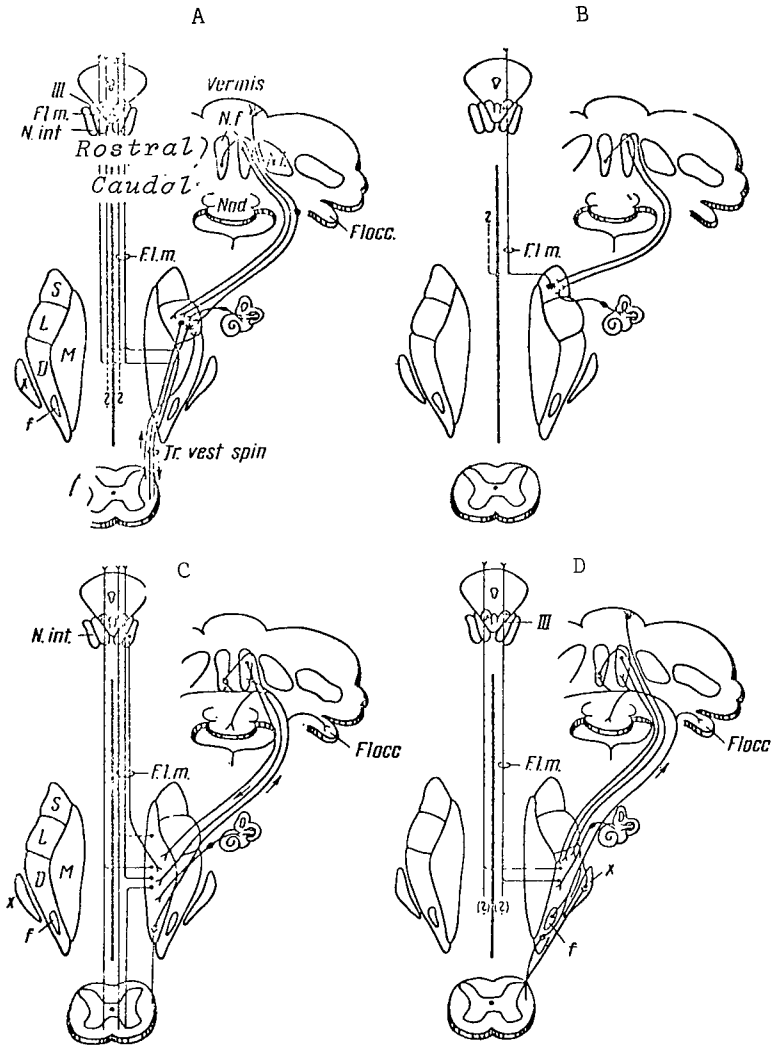

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Fig. 29. Simplified and Schematic Depiction of the Basic Afferent and Efferent Fibers of the Four Primary Vestibular Nuclei (Brodal et al., 1966).

(A) Basic Connections of the Lateral Vestibular Nucleus; (B) The Same of the Upper Vestibular Nucleus; (C) The Same of the Medial Vestibular Nucleus; (D) The Same of the Descending (Inferior) Vestibular Nucleus and of Groups *f* and *x*.

According to the assumption of G. P. Zhukova (1965) there may be a question here of the precise localization of objects in the surrounding medium, and the creation of images of their location on the basis of labyrinth stimuli, as I. S. Beritov described (1961). /98

The superior nucleus, both according to its neuron structure and by the nature of its connections, reveals a great similarity to the rostral portion of the complex of nuclei of the trigeminal nerve, and specifically to its main sensory nucleus. These two nuclei at definite levels of the trunk are apparently fused together, practically turning into one undivided formation. The indicated correlations evidently must be considered for the explanation of the mechanism, ensuring participation of fine proprioceptive and cutaneous stimuli (in the given case stimuli of the head regions) in the formation of vestibular reactions of the organism (Zhukova, 1965).

There are also bases to assume that the descending and medial nuclei, weakly differentiated from the reticular formation in the medial portion, connected primarily with the thin afferent fibers and forming efferent paths of a reticular type, are related to the perception of protopathic vestibular sensitivity, diffusely propagated further through the reticular formation. These nuclei can be compared with the more caudal portions of the complex of nuclei of the trigeminal nerve, i.e., with nuclei of the descending root, and also with the nucleus of the solitary tract. In addition, the lateral, more specific portion (in neuron structure) of the descending vestibular nucleus, together with the interstitial nucleus adjoining it, evidently is functionally close to the superior nucleus supplying perception of finer vestibular stimuli. Moreover, the features of structural resemblance, and, in places, even the fusion of this portion of the nucleus with the internal and external nuclei of the sphenoid bundle (Burdach's) can be presented in connection with the participation of fine proprioceptive and skin stimuli (in this case, the region of the trunk) in vestibular functions (Zhukova, 1965).

The remaining, larger portion of the descending nucleus and particularly the medial nucleus, basically consisting of reticular cells are represented, as one might conclude on the basis of comparison with other sensory formations of the brain stem and data on the conducting paths, as a structure through which protopathic vestibular sensitivity is mediated. The fact that the medial nucleus is inseparable from the adjacent section of the reticular formation, in which the afferents of the protopathic, somatic and visceral activity end, permits us to assume the participation of these types of sensitivities in the vestibular function and to present in, particular, a morphological basis for the vegetative component of vestibular reactions which is known in physiology. At the same time, in the descending and medial nuclei and primarily in the medial section of the medial nucleus, impulses from other portions of the brain can evidently be switched, in some way or another, /99

influencing the vestibular function. The latter concept was expressed by A. Brodal et al (1966) on the basis of the fact that in this part of the nucleus the efferent fibers, not from the labyrinth, but from various central sources, terminate from the cerebellum, from the upper sections of the brain and from the spinal cord. The data presented on the neuron structure of these nuclei, indicating, in particular, the parts of a large number of reticular neurons, especially in the medial nucleus, completely agrees with such a view, since these reticular cells usually serve as the place for switching impulses of various sources (Zhukova, 1965).

Reactions of the Neurons of Vestibular Nuclei to Adequate Stimulation of the Vestibular Apparatus, the Double Work of the Vestibular Apparatus

Responses of Neurons of the Vestibular Nuclei to Angular Accelerations

Adrian (1943) first recorded the discharges of specific neurons of the vestibular nuclei. Experiments were conducted on decerebrated cats lacking cerebellae under nembutal anaesthesia. The depth of electrode penetration was no more than 1 mm from the bottom surface of the 8 vestibules.

Adrian discovered units for which a more effective stimulus was rotation in a plane near to the horizontal and to responses of which neither inclinations of the head relative to the terrestrial vertical nor linear accelerations had any influence. With accelerated ipsilateral rotation, the activity of the units increased; contralateral rotation depressed their activity. Insofar as there are not only spontaneously active units, but also units which are silent at rest and discharging with almost constant frequency at all times, the author came to the conclusion that there is a wide diversity in the irritability of the vestibular neurons.

Also important is Adrian's observation that rotation in the frontal plane has an influence on units reacting to rotation in the sagittal plane, and inversely. The same units reacting to rotation in the horizontal plane were not subject to the influence of rotation in the frontal and sagittal planes, and at the same time rotation in the horizontal plane did not influence units reacting to rotation in these planes. Such canal interaction essentially differs from reactions obtained by Lowenstein and Sand /100 (1940) (cf. Table 4) in the skate, and possibly attests to further, more precise division of functions between the separate semicircular canals in the higher vertebrates.

With similar experimental conditions, actually under chloralose anaesthesia, Gernandt (1949) introduced a microelectrode

along the vestibular portion of the eighth nerve of a cat in the space between the internal acoustic meatus and the medulla oblongata and discovered, in addition to the units discovered by Adrian (Type I according to Gernandt) units which reacted with an increase (or decrease) in frequency of spontaneous discharge with rotation in both directions. Analogous data were obtained on rabbits by Eckel (1954) who registered the rhythm of neurons from the region of the vestibular nuclei.

Duensing and Schaefer (1958) discovered, in cats under light ether anaesthesia, one more type of neuron which reacted in an opposite way to Type I neurons: with ipsilateral acceleration, the activity of the neurons was suppressed; with contralateral, it was increased.

All the described experiments were characterized by the same insufficiency: they did not insure electrophysiological control of the elapsed applicability of the registered action potentials to secondary neurons of the vestibular nuclei, which introduced confusion in treating the results of investigations (Lowenstein, 1956; Gernandt, Gilman 1960).

Moreover, they did not expose quantitative regularities of the change in impulsation frequency of neurons with the action of adequate stimuli.

The excellent analytical studies conducted by Shimazu and Precht (1965, 1966) and Precht and Shimazu (1965) with the application of microelectrode technique on cats decerebrated at the intercollicular level did not have these insufficiencies.

The microelectrode was introduced into the brain stem under visual control 2.5 to 4 mm lateral of the central line and 3-6 mm caudal of the lower corpus bigeminum. The depth of the position of the majority of nerve units clearly reacting to horizontal angular acceleration and electrical stimulation of the vestibular nerve was from 1.5 mm dorsal up to 0.5 mm ventral of the standard point.[3]

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[3] On the scale of a micromanipulator the position of the microelectrode was noted, where its tip touched the central line of the bottom of the fourth ventricle 4-5 mm caudal of the lower corpus bigeminum. The coordinates of the tip of the electrode were calculated relative to this "standard point".

Histological analysis showed that injuries caused by the tip of the electrode were localized in the superior and medial vestibular nuclei, but sometimes in the lateral nucleus and the rostral portion of the descending nucleus.

With stimulation of the vestibular nerve by a single shock of /101
electrical current in the region of an ipsilateral vestibular nuclei, the summary elicited potential of the characteristic form was registered. It consisted of an initial positive-negative deviation (P) and a large (N_2) negative wave. The change in the amplitude of potential N_1 with a shifting of electrodes in the dorsal-ventral direction gave supplementary information on the shift of the electrode tip. Actually the amplitude of potential N_1 sharply diminishes (Fig. 30b) when the tip of the electrode intersects the border of the vestibular nucleus, especially its ventral border. As the histological control showed, the tip of the electrode was moved inside the vestibular nuclei, when the amplitude of the potential N_1 was greater than 1/3 or 1/4 of the maximum amplitude, obtained by single immersions of the electrode. With the application of this criterion, the intensity of vestibular nerve stimulation must be half the threshold for the generation of potential N_1, since with stronger stimulations in the ventral portions of the nuclei complex responses were registered, probably due to the superposition of the elicited potentials of the ponto-bulbar reticular formation (Gernandt et al., 1959).

With a single ventrical stimulation of the vestibular nerve in the ipsilateral vestibular nuclei, the elicited responses of specific neurons which were observed on a background of potentials N_1 and N_2 but never arose earlier than potential N_1, were registered in the form of action potentials with an amplitude of 0.3 to 1.2 mV.

The frequency of elicited discharges did not produce a rhythm frequency with an interval between stimulation of less than 5 msec (Fig. 31).

The latent period of commissure responses were not constant, and were distributed over a range from 0.1 to 8 msec and greater. These results attest to the fact that the elicited discharges belong to post-synaptic elements of the vestibular neuron, and do not appear as action potentials of the vestibular nerve's primary fibers.

Thus, in the studies of Shimazu and Precht (1965), for the identification of neurons, they considered the localization of neurons in the vestibular nuclei, histologically controlling the trans-synaptic response to electrical stimulation of the vestibular nerve, having indicated that commissure discharges were registered from secondary neurons of the vestibular nuclei and not from

primary fibers, and also a clear reaction to horizontal angular acceleration, and deceleration, indicated a functional connection between the registering nerve units and the receptors of the horizontal semicircular canals.

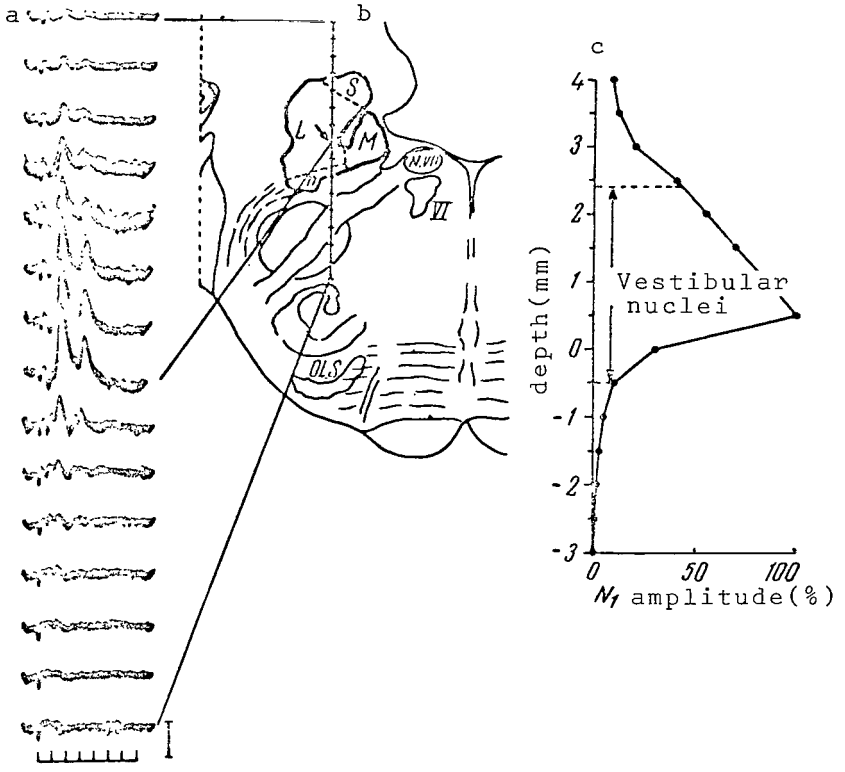

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Fig. 30. Elicited Potentials in the Vestibular Nuclei and Their Correlation with the Localization of the Electrode Tip (Shimazu, Precht, 1965).

(2) Summary Potentials Elicited by Single Stimulation of the Ipsilateral Vestibular Nerve. Deviations Upward Indicate Negativity of the Outgoing Potential. Each Records 20 Sweeps of the Ray. The Time Scale is 1 msec, Calibration 500 μV; (b) Schematic Drawing of a Cross Section of the Brain Stem Where Biopotentials were Registered. The Vertical Line Indicates the Depth of Immersion of the Electrode (Scale 500 μm); *S*, *L*, *M* and *D* are the Superior, Lateral, Medial and Descending Nuclei; *OLS* Superior Olive; *N* VII - 7th Nerve; VI - Nucleus of the 6th Nerve; (c) Change in Amplitude of the Potential N_1 with the Depth of the Immersion of the Electrode. The Zero Point of the Scale Corresponds to the Level of the Central Line of the 4th Ventricle's Bottom Surface. The Horizontal Dotted Lines Indicate the Superior and Inferior Borders of the Vestibular Nuclei.

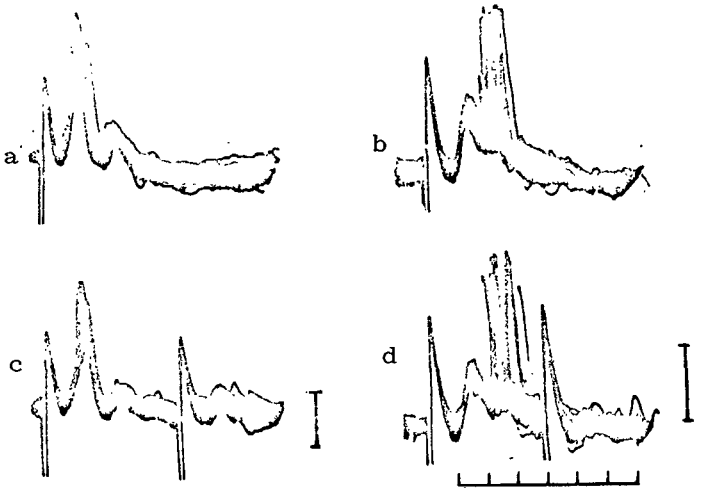

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Fig. 31. Responses of Neurons of the Vestibular Nuclei to Stimulation of the Ipsilateral Vestibular Nerve.

(a) All Spikes Superimposed on Potential N_1; (b) Responses of the Same Neuron to Paired Stimulation with an Integral of 4.4 msec; (c) Responses of the Other Neurons; the Spikes Are Superimposed on Potential N_1; (d) Responses of the Same Neuron to Double Stimulation with an Interval of 4.0 msec. Time Scale 1 msec, Calibration 500 μV. Each Recording was Obtained by the Superposition of 15 Ray Sweeps. The Original Positive-Negative Deviation on Each Recording is an Artifact of the Stimulation. (Shimazu, Precht, 1965).

Of 306 registered neurons reacting to angular acceleration in the horizontal plane, 205 showed an increase in discharge frequency with ipsilateral angular acceleration, and, if they possessed spontaneous activity, then with contralateral acceleration the discharge frequency decreased (Type I neurons). With 90 neurons the discharge frequency decreased with ipsilateral acceleration and increased with contralateral decelleration (Type II neurons).

In 10 neurons the discharge frequency increased with acceleration in both directions (Type II neurons).

In one neuron the discharge frequency decreased with acceleration in both directions (Type IV neurons).

Qualitatively, only the responses of Type I neurons were investigated.

102 out of 122 Type I neurons showed spontaneous activity. With rotation in the ipsilateral direction during constant angular acceleration, the frequency of spontaneous discharge in such neurons, as is shown in Fig. 32a, at first increases smoothly, attains the maximum and then remains unchanged despite continuing accelerated rotation. The maximum frequency value depends upon the amount of acceleration. After departure at a constant speed of rotation the discharge frequency smoothly decreased to the level of spontaneous activity. The authors called these neurons "tonic". The intracommissure intervals of tonic neurons are sufficiently constant. /104

In the remaining 20 neurons, spontaneous activity was either completely absent or only random discharges with a frequency less than 0.5 Hz were observed. As is shown in Fig. 32b, such neurons react to ipsilateral angular acceleration by a swift decrease in frequency from zero to a maximum value after a long latent period. With a departure at a constant speed of rotation, the decrease in the frequency is just as rapid. The authors called these neurons kinetic.

Intracommissure intervals of kinetic neurons, as distinguished from the tonic ones, are irregular. Mathematical analysis showed that in 2/3 of the Type I neurons the change in impulsation frequency with the action of constant ipsilateral angular acceleration is described by the equation

$$\nu - \nu_0 = (\nu_{max} - \nu_0) \cdot (1 - e^{-\frac{t}{\lambda}}), \qquad (1)$$

where λ is the time constant of the frequency response. This empirical equation corresponds in form with the theoretical equation (26) (Chapter II) describing the motion of the cupula under the action of constant angular acceleration, whereby λ corresponds to the time constant c/k of the semicircular canals.

In the remaining neurons the discharge frequency either was changed approximately according to the linear law or, after attaining maximum value, somewhat decreased. For such nonexponential changes, the period from the beginning of a change in frequency to the moment when this change attains a value ($\nu_{max} - \nu_0$) ($1 = 1/e$) is used as a convenient rough evaluation of λ.

The average value of λ of the tonic and kinetic neurons was, respectively, 8.1 ± 1.6 and 3.7 ± 0.8; moreover this difference is statistically reliable ($p < 0.01$). Values of λ measured during a decrease in discharge frequency after departure at a constant speed of rotation were approximately the same.

Mathematical analysis of the experimental data also showed that the dependency of the maximal change in discharge frequency of $\nu_{max} - \nu_0$ from the value of long-acting constant angular

acceleration (α) in a range of 0.5 - 19°/sec^2 is well approximated by the logarithmic function

$$v_{max} - v_0 = b \ln \frac{\alpha}{\alpha_0},$$

(2)

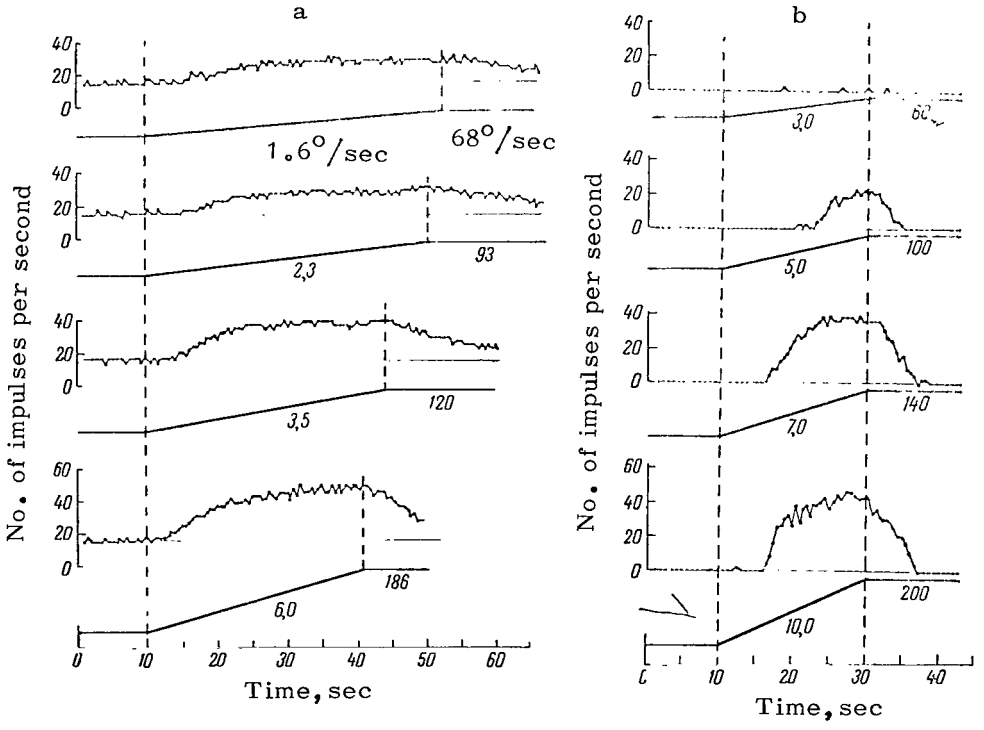

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Fig. 32. Change in Frequency of Tonic (a) and Kinetic (b) Vestibular Neurons with Ipsilateral Constant Angular Accelerations. Curves Under Each Frequency Diagram at Various Periods of Rotation. Slanted Portions are Periods of Acceleration, the Horizontal Ones Periods of Rotation with a Constant Speed, Numbers are the Values of Acceleration and Speeds (Shimazu, Precht, 1965).

where α_0 is the value of threshold acceleration; b the proportionality coefficient, or, if the dependence (2) is constructed in a semilogarithmic scale, the value of the tangent of the angle of inclination of a direct line to the logarithmic axis (Fig. 33). α_0 and b in (2) were defined for each unit after several rotations (usually 5-10) for various values of accelerations. /106

To avoid any systematic error with the definition of the threshold of α_0, the authors gave a number of accelerations with random distribution. When acceleration was applied near the threshold acceleration, the change in frequency was so small that it was almost impossible, especially with tonic neurons, to distinguish the response from spontaneous frequency fluctuations. Therefore a change in frequency greater than 5 Hz was accepted as a response.

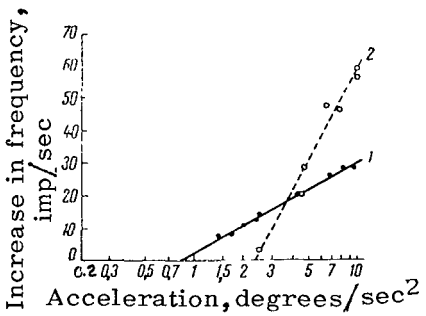

Fig. 33. Dependency of Maximum Change in Frequency on the Value of Angular Acceleration in Tonic (1) and Kinetic (2) Vestibular Neurons (Shimazu, Precht, 1965).

Strictly speaking, the dependencies (2) constructed in semilogarithmic scale (Fig. 33) are possibly not rectilinear in a region near the abscissa, and could be continued up to 0 °/sec^2. In this case no threshold would exist. As we have already noted, Groen et al. consider that in spontaneously active fibers of the ampullar nerve there is no threshold. However, in the experiments of Shimazu and Precht, statistically significant changes in impulsation frequency with acceleration lower than threshold acceleration were not observed in a majority of units. The lowest threshold found in the experiments was 0.23 °/sec^2.

The mean thresholds (α_0) of tonic and kinetic neurons were equal to 0.93 $\pm$ 0.55 and 4.65 $\pm$ 1.84°/sec^2. The values of the coefficient b defining the rate of change in frequency with an increase in the value of angular acceleration were equal to 31.6 $\pm$ 11.8 and 85.7 $\pm$ 30.5 °/sec, respectively. The difference between these values in both groups of neurons were statistically reliable ($p < 0.01$).

It is interesting that in two neurons with low spontaneous activity under the action of low-valued angular acceleration the discharge frequency decreased smoothly as in tonic neurons (large λ). Nonetheless they had high thresholds (α_0) and with great accelerations they showed a rapid change in frequency (small λ) /107

which is characteristic of kinetic neurons. Neurons of such mixed character possibly form an intermediate group of Type I neurons.

Thus in decerebrated anaesthetized cats the vestibular neurons of Type I fall into two distinct groups according to the nature of their response to adequate stimulation of the semicircular canals: kinetic and tonic neurons. Kinetic neurons are characterized by an absence of spontaneous rhythmic discharge, by high thresholds, by significant latency, by a rapid change in frequency with the action of constant angular acceleration and by an abrupt growth in maximum discharge frequency with a growth in the value of acceleration. Tonic neurons have the opposite characteristics. Because of the absence of spontaneous discharge, kinetic neurons are found to be more complex than tonic neurons. Therefore the ratio of the usual number of tonic and kinetic neurons found in the experiments of Shimazu and Precht (1965), 5:1, probably is not representative of actual neuron populations.

As was indicated in Chapter II, with an indefinitely long rotation under constant angular acceleration, the cupula is deflected and angle $\theta_{max} = \alpha \cdot \frac{I}{k}$ [cf. (6) Chapter II]. Comparing this expression with the empirical equation (2), it is possible to extract the correlation

$$\nu_{max} - \nu_0 = b \ln \frac{\theta_{max}}{\theta_0}, \qquad (3)$$

where θ_0 is the deflection of the cupula corresponding to the threshold acceleration; i.e., the maximum change in frequency with long-lasting angular acceleration proportional to the logarithm of the maximum deflection of the cupula.

A logarithmic relationship (3) between the neuron's maximum change in frequency and the acceleration was made in a range of accelerations from 0.5 to 10-17°/sec^2.

As was indicated in Figure 32, both the tonic and kinetic vestibular currents usually preserved the maximum discharge frequency unchanged over a prolonged period of the action of constant angular acceleration, ie. tendencies toward adaptation did not appear.

However, in 1/5 of all registered neurons the discharge frequency decreased somewhat after attaining a maximum value, despite continuing accelerated rotation. These neurons showed a clear overlapping of the spontaneous discharge frequency when the platform suddenly stopped after prolonged (3 min) rotation at a constant speed. In several cases the discharge frequency then not only returned to the rest level, but even exceeded it. In kinetic neurons, overlapping was usually not observed due to the absence of

spontaneous discharge, but a consequent appearance of discharges was observed.

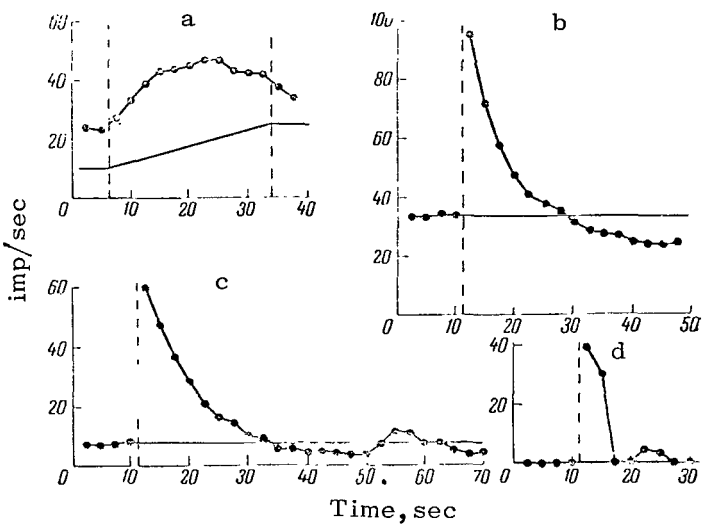

Fig. 34. Different Models of Frequency Responses of Singular Vestibular Neurons. /108

(a) Response of a Tonic Neuron to Ipsilateral Angular Acceleration ($7°/sec^2$). Vertical Dotted Lines Indicate the Beginning of Acceleration and the Moment of Departure at a Constant Speed (195°/sec); (b,c) Responses of Tonic Neurons to Stop Stimulus (b: 100°/sec; c: 65°/sec); (d) Response of a Kinetic Neuron (150°/sec) with Contralateral Rotation. (a-b) Were Obtained From Animals with a Destroyed Contralateral Labyrinth (Shimazu, Precht, 1965).

Neurons which preserved a maximum frequency during extended action of acceleration without any adaptation did not show overlapping after a sudden stop of rotation and, on the other hand, neurons which decreased the discharge frequency showed a pronounced overlapping to some degree or a damping oscillation after stopping (Fig. 34). Then it would be possible to suppose that the observed decrease in frequency during acceleration is not an actual adaptation, but only the initial phase of this oscillation.

It remained unclear whether damping oscillations of discharge frequency around the rest level were elicited by the peripheral mechanism or by the activity of the central nervous system. It is interesting that Groen at al. (1952) observed a similar phenomenon

in primary fibers of the ampullar nerve of a skate after application of stop-stimuli.

The contralateral labyrinth, as the author indicated, is not /109
responsible for oscillations since oscillations were observed even after its destruction.

Thus the experiments of Schimazu and Precht (1965) did not give convincing proofs of the existence of any significant adaptation in Type I neurons when long-lasting constant angular acceleration was used as an adequate stimulation of the terminal organs of the semicircular canal, which agrees with the assumptions of Ross (1936) and Adrian (1943), and also with the data of Crampton's investigations (Crampton, 1965) on neurons of the vestibular nuclei in a cat.

Lowenstein (1965) investigated the action of galvanic polarization and discharge of impulses from the terminal organs of the horizontal semicircular canal of the skate. He showed that with exponential increase in the value of the stimulation current (which simulated a deflection of the cupula with the action of constant angular acceleration) the discharge frequency adapts very slightly. On the other hand, with the inclusion or exclusion of current, the discharge frequency at first sharply changes, but afterwards a significant and rapid adaptation is observed. The response of the tonic and kinetic neurons is similar to the response of terminal organs of the semicircular canal to slowly increasing polarizing current. Possibly if the cupula is swiftly deflected and held in a deflected position, adaptation will be observed. To a certain degree, the results of Ledoux's studies (1961) are explained by a similar phenomenon.

The Functional Connections of Type I Neurons with Primary Vestibular Afference

As Shimazu and Precht (1965) indicated, the elicited potential of the vestibular nuclei in response to a single electrical stimulation of the ipsilateral vestibular nerve consists of a positive or positive-negative wave (P), a large negative wave (N_1) and a small delayed negative wave (N_2). The latent period of the potential P, measured from the index of the artifact of stimulation to the top of the positive wave, was 0.66 ± 0.14 msec (Precht, Shimazu, 1965), and can indicate the moment of arrival of the afferent impulses at the axon terminal (Brooks, Eccles, 1947). The potential P reproduces a rhythm of nerve stimulation with a frequency of up to 200 Hz without any visible changes in amplitude, is resistant to nembutal anaesthesia and increases in amplitude, when the microelectrode is introduced into the medulla oblongata near the entrance of the 8th nerve. Thus the potential P reflects the total elicited commissure activity, chiefly of the primary vestibular nerve elements, although antidromic responses of the afferent fibers to the

terminal organ probably are also included in the summary potential (Gacek, 1960). A more pronounced component of the elicited summary /110 potential is the potential N_1, the amplitude of which sometimes exceeded 1 mV. The latent period of the potential N_1 is 1.06 $\pm$ 0.22 msec; i.e., it rises in approximately 0.4 msec after the arrival of afferent impulses at the axon terminal. The duration of the potential is 1 - 1.5 msec. With rhythmic stimulation of the vestibular nerve at a frequency of 30 Hz, the amplitude of the potential decreased to 70% for 1 sec and to 40% with a stimulation at a frequency of 100 Hz. The full restorative period of the potential was around 10 msec. With deep nembutal anaesthesia the potential N_1 almost completely disappeared and was replaced by a slow negative wave of small amplitude, representing possibly the synaptic potential of the vestibular neurons (Brooks, Eccles, 1947). Thus the potential N_1 reflects the summary monosynaptically elicited commissure activity of the neurons of the vestibular nuclei.

The latent period of the potential N_2 is 2.46 $\pm$ 0.26 msec, the duration 2 - 3 msec or more. With rhythmic stimulation of the vestibular nerve at a frequency of 30 Hz the amplitude of the potentials decrease 40%, and with stimulation at a frequency of 100 Hz, to 15%; i.e. potential N_2 is more sensitive than N_1 to high frequency stimulation. The complete restorative period lasted more than 20 msec. The potential N_2 is more sensitive than the potential N_1 both to nembutal anaesthesia and to the physiological conditions of the animal.

With stimulation of the vestibular nerve, the elicited summary potentials are registered not only in the ipsilateral vestibular nuclei but also in the ventrally located pontobulbar reticular formation. Since the response of the reticular formation has a threshold higher than the thresholds of any component (P, N_1 and N_2) of the elicited response in the vestibular nuclei, it is possible to conclude that the summary potentials N_1 and N_2 were produced by an internal mechanism of the vestibular nuclei and not by a reticular formation.

When the vestibular nerve was stimulated during contralateral rotation at a constant speed (200°/sec) by weak current impulses, small N_1 and N_2 potentials were registered. After cessation of rotation the potential N_1 noticeably increased, while the potential N_2 decreased insignificantly.

Thus the neural mechanisms responsible for the origin of the potential N_1 are more sensitive to the action of adequate stimulation of the labyrinth than the mechanisms responsible for the potential N_2.

We recall that all the nerve units described in this section are second order neurons of the vestibular nuclei, which increased the impulsation frequency with the lateral angular acceleration and, if they possess spontaneous activity, decrease the discharge frequency with contralateral acceleration. Thus they show a Type I response to rotation (Gernandt, 1949; Duensing, Schaefer, 1948; Shimazu, Precht, 1965). Insofar as such a type of response is completely identical to the impulse activity of the primary afferents /111
from the ipsilateral horizontal semicircular canal (Lowenstein, Sand, 1940 a and b; Ledoux 1949 at al.). It is no surprise that all these neurons are excited by electrical stimulations of ipsilateral primary vestibular fibers and not one of them manifested inhibition.

The majority of kinetic neurons of the ipsilateral vestibular nuclei were excited by stimulation of the vestibular nerve with sufficient stable latent periods of elicited discharges which always appeared against the background of the summary potential N_1. Even with minimal intensity of stimulation, the duration of latent periods was small: 1.2 to 2 msec, i.e. action potentials arose in 0.6 ~ 1.4 msec after the arrival of nerve impulses at the axon endings of primary neurons. With a stronger relationship, discharges of the nerve arose with a retardation of 0.4 to 0.8 msec. A small value of synaptic retardation and its insignificant fluctuation attests to the fact that kinetic neurons are activated chiefly monosynaptically by primary afferent impulses. Such a conclusion agrees well with the characteristic of monosynaptic SPSD neurons of the lateral vestibular nucleus elicited by stimulation of primary vestibular afferents (Ito, et al., 1964), and also with anatomical investigations of the connection between the primary fibers of the vestibular nerve and neurons of the vestibular nuclei (Walberg et al., 1958).

Responses of the majority of tonic neurons, registered only in the absence of anaesthesia, with minimum intensity of stimulation had comparatively prolonged latent period with great scattering: 1.5 - 8.5 msec. Such a neuron reaction may be elicited by slow, retarded depolarization of neurons of the vestibular nuclei in comparison with short, latent, deep depolarization of monosynaptic SPSP (Ito et al., 1964).

It is possible that the prolonged latent period of tonic neuron excitation after a single stimulation of the vestibular nerves is explained by the low speed of impulse conduction along the primary afferent fibers, providing excitation of tonic neurons. Actually, activation of the two groups of Type I neurons by afferent fibers of various diameters is completely probable, insofar as the spectrum of diameters of single fibers of the vestibular nerve is sufficiently broad: in the guinea pig it is 1-9 μ (Wersall, 1956).

However Precht and Shimazu (1965) showed that the threshold intensities of electric stimulation of the vestibular nerve for

the excitation of tonic and kinetic neurons do not differ in practice. Furthermore, several tonic neurons were excited by very weak stimuli near the excitation threshold of primary afferent fibers (*P*-potential). Consequently having only the basis of differences in the speed of conduction of afferent fibers makes it difficult to explain the prolonged latency of tonic neuron activation. /112

The authors consider that it is possible that a prolongation of the latent period is explained by differences of synaptic contacts of the primary afferents with tonic and kinetic neurons.

Walberg et al. (1958) and Brodal et al. (1966) showed that the primary vestibular fibers to the lateral vestibular nucleus abundantly connect the dendrite processes of small cells and also end at the surface of the pericarion. Possible this is true even for other vestibular nuclei (Brodal et al., 1966).

Fadiga and Brookhart (1960) found that in the from the SPSP of motor neurons elicited monosynaptically through axodendrite synapses from fibers of the dorsal roots has a more prolonged development in time than the axosomatic SPSP from fibers of the lateral column. These effects were observed even under membutal anaesthesia. Therefore the prolonged latent period of tonic neuron excitation could be explained by the slow increase in depolarization through axodendrite synapsis. However, in the experiments of Precht and Shimazu (1965) after the introduction of nembutal which, as is known, suppressess the multisynaptic transmission, no synaptically significant difference was found in the characteristics of the impulses and duration of latent periods between kinetic and tonic neurons in response to stimulation of the vestibular nerve. Therefore the second assumption does not explain the obtained results. The existence of multisynaptic connections in the vestibular nuclei (Ito, et al., 1964), in the opinion of Precht and Shimazu, best explains the long latent period of tonic neuron activation after weak, single stimulation of the vestibular nerve.

The retarded response can be elicited by a slow increase in depolarization of the tonic neuron which is created by retarded and synaptic bombardment collected through multisynaptic paths. When the stimulation intensity increased, discharges were observed even with small stable latent period and retarded discharges, so that the tonic neurons even have monosynaptic connections. With weak stimulation not only were monosynaptic discharges and retarded discharges observed, but also secondary retarded discharges. These latter discharges were elicited probably also by the retarded synaptic bombardment (Hunt, Juno, 1959). The fact that small doses of nembutal eliminated only these retarded discharges strengthens the concept of the multisynaptic origin of retarded commissures.

The response of kinetic neurons to vestibular nerve stimulation is similar to the response of tonic neurons under nembutal /113

anaesthesia; i.e., multisynaptic mechanisms appear relatively less important in the activation of kinetic neurons than tonic ones. Besides the well-established monosynaptic paths in the spinal cord dividing the reflex of extensions, Granit et al., (1957) assumed the principle of multisynaptic activation of tonic motor neurons. Correspondingly, excitation with a long latent period from muscular afferents with low thresholds in the tonic motor neurons of the spinal cord, was discovered while the phase motor neurons were excited only monosynaptically (Tsukhara, Ohye, 1964).

As possible anatomical substrata for multisynaptic excitation of the vestibular nerves can be only the intercalory neurons in the vestibular nuclei or the colateral axons, leaving the vestibular nuclei (Brodal et al., 1966; Lorente de No, 1933b). Vestibular connections (Gernandt et al., 1959) probably are not essential for multisynaptic mechanisms, since activation of tonic neurons with a long latent period was caused by stimulation intensity of the vestibular nerve which was significantly less than that necessary for reticular responses.

Since in the experiments of Precht and Shimazu the cortex of the cerebellum and fastigial nuclei were separated out, the possibility of including the cerebellum in multisynaptical excitation of the vestibular nuclei neurons (Brodal, et al., 1966) was removed.

The absence of monosynaptic excitation in several tonic neurons might be explained by the fact that, as histilogical data show, definite regions in the vestibular nuclei are deprived of vestibular afferents (Walberg et al, 1958). Insofar as many tonic neurons were excited monosynaptically and multisynaptically with weak stimulation of the vestibular nerve, it is improbable that all tonic neurons are distributed in regions free from primary vestibular afferents. Actually tonic and kinetic neurons are clearly distributed side by side (Shimazu, Precht, 1966).

Mickle and Ades (1954) registered, in the vestibular nuclei of the cat with stimulation of the vestibular nerve, an elicited potential, the components of which had latent periods of 1 - 1.25 and 4 msec which correspond to the latent periods of the potentials N_1 and N_2. The characteristics of the potentials N_1 and N_2 (latent period, sensitivity to nembutal anaesthesia and to horizontal angular acceleration) were, respectively, the same as in kinetic and tonic neurons. Consequently the component N_2 of the elicited potential reflects the total activity of tonic neurons, which are /114 activated through multisynaptic chains. The described experiments make it possible to assume that multisynaptic mechanisms are essential for maintaining spontaneous activity of tonic vestibular influences.

Inhibition of the Central Vestibular Neurons From the Contralateral Labyrinth and its Conducting Paths

With a single stimulation of the vestibular nerve, the elicited potential is registered not only in the ipsilateral vestibu-

lar nuclei but also in the contralateral ones (Shimazu and Precht, 1966), where it consists of an initial positive deflection and a subsequent negative one (Fig. 35).

The amplitude of the initial positive deflection is on the order of 50-75 μV (maximum 100 μV); the latent period measured from the artifact of stimulation to the crest of the positive wave is 2.4 - 2.5 msec (Fig. 35b).

Summary elicited potentials in the contralateral vestibular nuclei are discovered in a clearly localized region. In Figure 35a the shaded area indicates the region where the amplitude of elicited potentials consists of more than 30% of the maximum amplitude of the initial positive potential. The region is localized in the ventral portion of the medial nucleus and in the ventral-medial portions of the superior and lateral nuclei. In the rostral-caudal direction these elicited potentials were observed primarily in the knee of the facial nerve, in the medial and superior nuclei and gradually lowered to the rostral border of the superior nucleus. The elicited potentials were not observed in the caudal halves of the medial and descending nuclei. Figure 36a represents the elicited potentials at various points of a cross section of the brain stem in response to single stimuli of the vestibular nerve. In the ventral-lateral portion of the ipsilateral vestibular nuclei there was registered, as was described above, a large presynaptic potential peak of primary fibers of the vestibular nerve and a small potential N_1 and N_2. When the electrode was introduced into the brain stem along the central line, a three-phase potential was registered: a small positive deflection preceded the negative-positive deflection. The latent period of the negative component consisted of 2-2.1 msec. The negative potential often had two peaks. This potential was registered exclusively in the dorsal portion of the brain stem no deeper than 1.5-2 mm. With the doubled stimuli at an interval of 5 msec, the response to the second stimulus was noticeably suppressed (Fig. 36b), which is similar to the characteristics of N_1 registered in the ipsilateral vestibular nuclei, but differs from the characteristics of the summary elicited potential of primary afferents which produce a stimulation frequency up to 500 Hz.

Thus, a three-phase potential, registered in the dorsal portion of the brain stem along the central line, reflects the summary elicited activity, conducted along fibers, originating from the secondary vestibular neurons on the ipsilateral side, and not directly from primary vestibular afferents.

When the microelectrode was introduced into the ventral-medial portion of the contralateral vestibular nuclei, an initial positive potential was registered. This potential reacted the same as potentials N_1 and N_2 to double stimulation of the vestibular nerve, which indicates its transynaptic origin. The authors did not discover any positive data on the existence of cross-primary fibers to the contralateral vestibular nuclei, which agrees with the anatom-

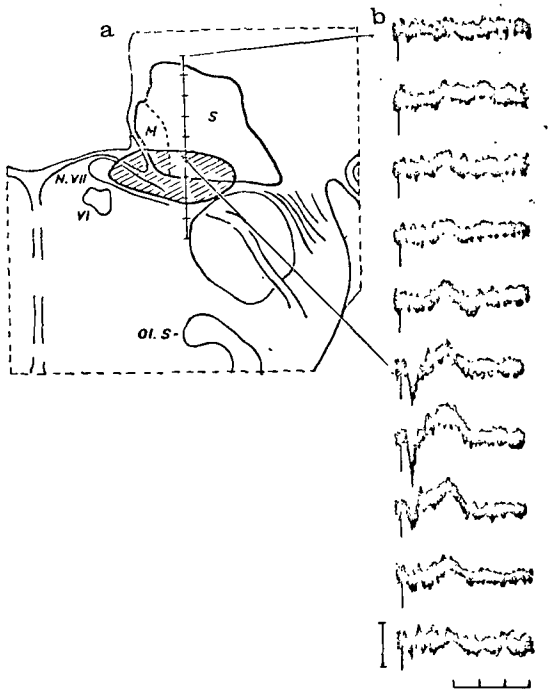

Fig. 35. Elicited Potentials of the Contralateral Vestibular Nuclei. /115 (2) Schematic Drawing of a Histological Section. The Vertical Line Indicates the Position of the Electrode Tip; Scale 500 μ; In the Shaded Areas, Potentials with an Amplitude Greater than 30% of the Maximum Amplitude of Positive Potential Were Registered. The Remaining Designations are the Same as in Figure 30. (b) Summary Potentials Elicited by Single Stimulations of the Vestibular Nerve. The Intensity of Stimulation 1.2 V (2 Times Greater than the Threshold of N_1). Each Recording Was Registered at a Point Indicated by Labels of Scale A and Obtained by the Superposition of 10 Ray Sweeps. The Time Scale is 5 msec, Calibration 100 mV (Shimazu and Precht, 1966).

ical data of A. Rassmusen (1932). The latent period of the initial positive potential equals 2.4 - 2.5 msec, which is 0.4 msec longer than the latent period of the potential registered along the central line of the brain stem. The latency of antidromic discharge of Type I neurons equals 0.3 - 0.4 msec after a single stimulation, applied along the central line of the brain stem (Fig. 36 e, A and B). Hence it follows that the initial positive potential, which is localized in the ventral-medial portion of the contralateral vestibular nuclei, is produced by nerve impulses propagated along the commissural fibers and passing under the bottom surface of the fourth ventricle.

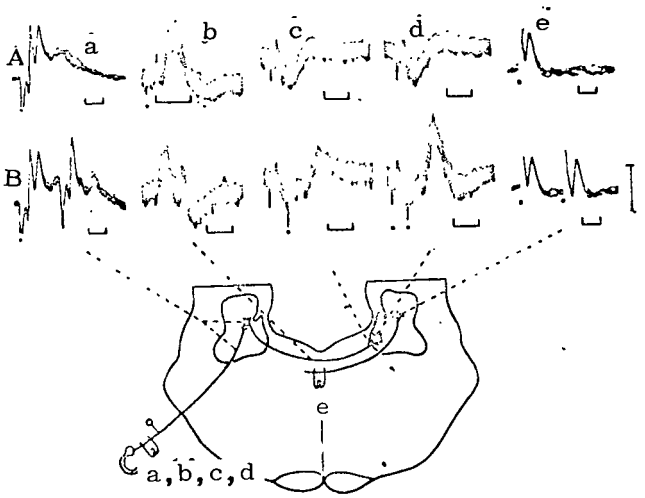

Fig. 36. Elicited Potentials in Various Portions of the Conducting Path From the Ipsilateral to the Contralateral Vestibular Nuclei. (A) Response to Single Stimulation; (B) The Same to Double Stimulation; (a) Active Electrode in the Ventral Portion of the Ipsilateral Vestibular Nuclei; (b) Along the Central Line (0.5 mm Below the Bottom of the Fourth Ventrical); (c) and (d) in the Ventral Portion of the Contralateral Vestibular Nuclei; (e) Antidromically Elicited Commissures of Type I Vestibular Neurons in Response to Stimulation of the Dorsal Portion of the Brain Stem Along the Central Line. The Moment of Stimulation is Indicated Below the Oscillograph Point. The Stimulation Intensity was 2 Times Less Than the Threshold of N_1 (for a-d); for (e) it was 0.4 V. Time Scale: 1 msec for (a) and (e) and 5 msec for (b), (c) and (d). Calibrations: (a), (e) = 600 and (b), (c) and (d) = 100 μV. The Lower Diagram Indicates the Point of Stimulation and Also Structures Connecting the Elicited Potentials (Shimazu and Precht, 1966). /116

The arrival of the very first impulses in the ventral portion of the nuclei can be approximately characterized by the peak of the positive potential (Brooks, Eccles, 1947; Eccles 1966). The character of the change in amplitude of the contralateral positive potential with the increase in stimulation intensity is similar to a change in amplitude of the ipsilateral potentials N_1 and N_2) but differs from the elicited potentials of the reticular formation (Fig. 37). The threshold of the positive potential is definitely lower than the threshold of potentials of the reticular formation. These data also support the point of view that the elicited contralateral potentials reflect the activity of the ipsilateral vestibular nuclei and not the activity of the reticular formation.

With a single stimulation of the vestibular nerve it is often difficult to separate the subsequent slow negative component of the elicited contralateral potential (Fig. 36a, d). Double stimu-

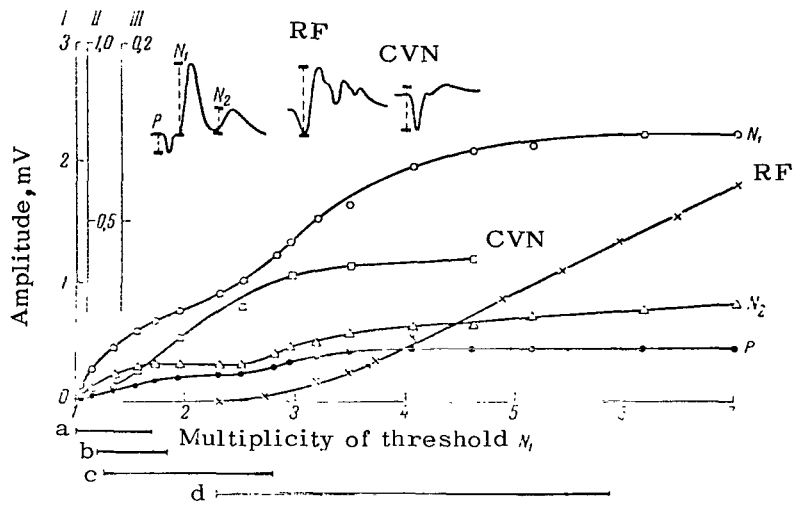

Fig. 37. Connection Between Summary Potentials and Responses of Single Neurons. /117
The Upper Figure: Amplitudes of Potentials P, N_1 and N_2 of the Reticular Formation (RF) and Contralateral Vestibular Nuclei (CVN). (a) Excitation Threshold of Type I Neurons With Stimulation of the Vestibular Nerve; (b) Excitation Threshold of Type II Contralateral Neurons; (c) Inhibition Threshold of Type I Contralateral Neurons; (d) Stimulation Threshold of Type I Contralateral Neurons After Medial-Dorsal Section of the Brain Stem. Thresholds Were Defined with a Stimulation Frequency of 50 Hz. Scales of Amplitude: *I* - for P, N_1 and N_2; *II* - RF; *III* - CVN (Shimazu, Precht, 1966).

lation, however, elicited a large negative summary potential with a latent period of 3.2 msec after the second stimulation (Fig. 36D, d). These results indicate that some vestibular neurons are excited by impulses conducted along the commissural fibers. The negative potential is more pronounced in the ventral-medial portion of the vestibular nuclei, although it is more dorsal than the region where a sharp positive potential of commissural fibers (Fig. 36) was registered, which corresponds with the localization of Type II neurons which are excited (as will be described below) through commissural fibers. /118

After section of the brain stem along the central line from the inferior corpus bigeminum to the obex, the initial positive potential and the subsequent negative component markedly diminished or even completely disappeared (Fig. 40). Figure 40 also illustrates the results of histological investigation indicating the depth of section necessary to eliminate elicited contralateral potential. An incision represented by the black region only slightly decreased

the elicited contralateral potentials, while destruction of the shaded area completely eliminated the potential. Hence the conclusion: in order to remove the contralateral elicited potentials, it is necessary to make a central section of the brain stem the depth of around 2 mm and to somewhat broaden it in the direction of the medial longitudinal bundle. Insofar as responses of vestibu-

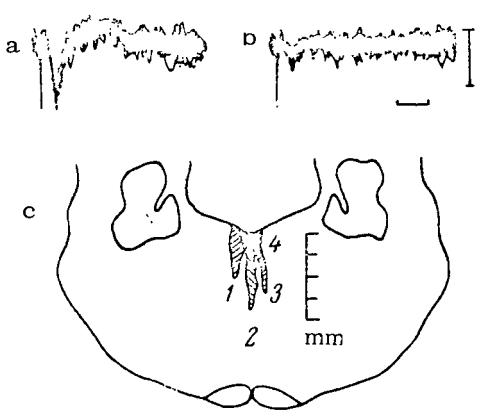

Fig. 38. Influence of a Medial-Dorsal Section of the Brain Stem on the Contralateral Elicited Summary Potentials of the Vestibular Nuclei. (a) Control Responses; (b) After Section (Shaded Area 1); (c) Scheme of Histological Cross Section of the Brain Stem Indicating the Depth of Section. Elicited Contralateral Potentials Almost Completely Removed by Section 1-3 and Insignificantly by Section 4. Each Recording was Made by the Superpositions of 15 Ray Sweeps (Shimazu, and Precht, 1966).

lar units to natural and electrical stimulation of the ipsilateral /119
vestibular nerve were the same after the section as before injury, the change in summary potential is not connected with the general depression of activity of the brain stem caused by injury. These data serve as one more proof of the fact that summary potentials in contralateral vestibular nuclei reflect the activity of ipsilateral neurons, conducted along commissural fibers and passing under the bottom of the fourth ventricle.

With strong stimulation of the vestibular nerve in the contralateral vestibular nuclei, the elicited summary potentials having a complex multiphase form and 100-200 μV in amplitude observed. Such types of potentials were especially pronounced in the underlying reticular formation, attesting either to the functional or physical distribution of the reticular formations response to the vestibular nuclei. A medial section of the dorsal portion of the brain stem did not change these potentials.

Inhibition From the Contralateral Labyrinth of the Type I Vestibular Neurons

In 53 of 59 Type I tonic neurons identified in response to horizontal angular acceleration, spontaneous discharge was suppressed by weak rhythmic stimulation (300 - 100 Hz) of the contralateral vestibular nerve. The intensity of stimulation, in addition, was lower than the threshold for elicited potentials in the pontobulbur reticular formation. In six of the neurons inhibitory influences appeared to be weak. In the kinetic neurons, the effects of stimu-

lating the contralateral nerve were investigated on discharges elicited by rotational stimulation or by electrical stimulation of the ipsilateral vestibular nerve. In each test the discharges of the kinetic neurons were also suppressed by stimulation of the contralateral vestibular nerve. Excitation was not observed in any Type I neurons with weak stimulation of the contralateral nerve, subliminal for the elicited potentials of the reticular formation.

With a medial section of the brain stem, cross-inhibitory influences were completely removed. With stimulation sufficiently strong to produce responses in the reticular formation, exciting contralateral responses were observed. The depth of the section necessary for complete removal of contralateral suppression of Type I neurons was 1.5-2 mm, which corresponds to the depth of the section removing elicited summary contralateral potentials.

Figure 37 represents the connection between the amplitude of /120
some potentials and single neuron responses. In this diagram the amplitude of summary potentials in various portions of the brain stem elicited by single stimulation of the vestibular nerve are traced as a function of the intensity of stimulation expressed in threshold values of the potential N_1. Given such a concept, the connection between the amplitude of the elicited potential and the intensity of the stimulus corresponded for various animals and did not depend on the absolute value of the threshold stress, which was influenced by the conditions of the stimulating electrode's contact with the vestibular nerve. The curves of the change in amplitude of potentials of P, N_1 and N_2 abruptly increase with the value of the intensities of the stimulus by 2 1/2 times greater than the threshold of the potential N_1. This intensity corresponds to the minimal value of stimulation necessary for eliciting potentials in the reticular formation, the value of which increases in amplitude with a stronger stimulation even after the amplitudes of the potentials N_1 and N_2 attain the maximum. These results indicate that at this moment the finest primary fibers of the vestibular nerve are activated, which sharply increases the responses of the vestibular nuclei and leads to the appearance of the response in the reticular formation. The multipeaked potential P, which can be produced by fibers having various conduction speeds, was not observed by the authors with any intensity of stimulation, probably due to the small path of conduction and small amplitude of the potential P.

Figure 37 shows the ranges of threshold values for stimulation of the vestibular nerve necessary to excite or to inhibit various vestibular neurons under different conditions. The excitation thresholds of the ipsilateral tonic and kinetic Type I neurons fluctuated from 1 to 1.7 and are indicated by the black horizontal line a. Thresholds for inhibition of contralateral Type I neurons fluctuated from 1.25 to 2.8 (line b). Inside this range of intensities of stimulation the summary potentials in the contralateral vestibular nuclei are sufficiently well-developed, while in the reticular formation not even weakly developed elicited potentials are discovered. For excitation of the contralateral Type I neurons

after medial section of the brain stem, a very strong stimulation having a value from 2.3 to 5.9 was necessary, as was indicated by line d in Figure 37. This band of stimuli corresponds to the intensity of stimulation necessary to activate neurons of the reticular formation. Even with intact commissural fibers, stimulation 4-5 times above the threshold of the potential N_1 elicited excitation of the contralateral Type I neurons. Evidently strong activation of the reticular vestibular connections can overcome inhibitory influences being manifested through the commissural fibers.

After complete unilateral destruction of the labyrinth, discharges of Type I neurons on the intact side were registered and thresholds to ipsilateral horizontal angular acceleration were defined. The maximum increase in frequency $\nu_{max} - \nu_0$, as in animals with intact labyrinths, was proportional to the logarithms of acceleration. However thresholds of the change in frequency of tonic vestibular neurons during horizontal acceleration fluctuated from 0.8 to 3.5°/sec^2 (2.12 $\pm$ 0.91°/sec^2) and were noticeably (p <).01) higher than the case of both intact labyrinth (0.65 $\pm$ 0.25°/sec^2) (Shimazu, Precht, 1965). The authors associate these results with removal of the inhibitory cross-influences from the contralateral semicircular canal. The frequency of spontaneous discharges was somewhat higher than with both labyrinths intact, although statistically it was insignificant. /121

Discharges of the vestibular nuclei neurons were registered, even on the side with destroyed labyrinth. In addition, the frequency of spontaneous discharges and the probability of removing them were much less than on the intact side, although with electrical stimulation of the proximal end of the severed vestibular nerve, elicited discharges were registered in many neurons on the side of the destroyed labyrinth. An investigation of the response of more than 100 vestibular units identified by stimulation of the vestibular nerve (Schimazu, Precht, 1965) showed that obtaining a clear Type I response to horizontal angular acceleration of the vestibular nuclei neurons on the destroyed side was extremely difficult. Only an insignificant number of units replied with weak Type I responses during very high angular accelerations (more than 100°/sec^2 with a duration of 1 sec) which corresponds with the data obtained earlier (Gernandt, Thulin, 1952).

Excitation from the Contralateral Labyrinth of the Vestibular Type II Neurons

The discharge frequency of Type II neurons decreased in response to ipsilateral horizontal angular acceleration and increased approximately exponentially during contralateral angular acceleration, thus indicating characteristics similar to Type I neurons, but oppositely directed (Shimazu, Precht, 1965).

For many Type II neurons there was established, as for Type I neurons (Shimazu, Precht, 1965) a logarithmic connection between maximum change in discharge frequency and the value of constant angular acceleration. Thresholds of Type II neurons to horizontal angular acceleration of 1.5 - 100 °/sec^2 were usually significantly higher than the thresholds of Type I neurons (0.23 - 1 °/sec^2) (Shimazu, Precht, 1965).

After unilateral destruction of a labyrinth, on the destroyed /122
side Type II neurons which finally reacted to angular acceleration were discovered as before, in contrast to the absence of Type I responses. The sensory input which produced Type II responses under the given experimental conditions can be defined only by contralateral horizontal canals. Consequently Type II neurons are excited by stimulation of the contralateral semicircular canals. This conclusion is also confirmed by the fact that the majority of Type II neurons (40 out of 42) were excited by electrical stimulation of the contralateral vestibular nerve. Such excitory responses markedly contrast with the inhibitory responses of Type I neurons to identical stimulation.

The frequency of spontaneous discharge of Type II neurons fluctuated within the bounds of 0 - 30 Hz, as for Type I neurons.

The shortest latent period of first spikes equalled 3.2 msec, which corresponds with the latent period of the subsequent negative elicited potential (Fig. 32b). If this value is compared with results described above, it is possible to come to the conclusion that Type II neurons are excited with contralateral stimulation of the vestibular nerve for 0.7 msec after the arrival of impulses along the commissural fibers and for 0.8 msec before the beginning of inhibition of Type I neurons.

Thresholds of Type II neurons with stimulation of the contralateral vestibular nerve were 1.2 - 1.85 times higher than the threshold of potential N_1 (band pass b on Fig. 37). These intensities are somewhat higher than those necessary for activation of ipsilateral tonic and kinetic Type I neurons (band pass a) but not for contralateral inhibition of Type I neurons. Therefore it is assumed that excitation of contralateral Type II neurons is also manifested by means of commissural fibers under the bottom of the fourth ventricle and not by the reticular vestibular connection. Such a point of view is strengthened by the fact that no Type II neuron was excited with weak stimulation of the contralateral vestibular nerve after section of the commissural fibers.

The majority of Type II neurons which were excited by weak stimulation of the contralateral vestibular nerve were localized in the ventral portion of the medial nucleus and in the ventral-medial portion of the superior nucleus although a small number were discovered even in the central and dorsal portions of the nuclei. This region corresponds with the region where elicited

potentials (following negative components) were chiefly registered. The authors note that commissural amplitudes of Type II neurons are usually less than 200 μV, while the amplitudes of discharges of tonic Type I neurons equal 300 - 900 and kinetic 500 - 1500 μV.

Effect of Stimulation of the Ipsilateral Vestibular Nerve on Type II Neurons

From 61 registered Type II neurons, 31 were not activated with /123 stimulation of the ipsilateral vestibular nerve. Even with an intensity of stimulation 4-5 times greater than the threshold N_1, these units were not directly activated after each stimulation, but showed only a diffusely increased discharge frequency during high frequency stimulation, possibly through the activation of reticular formation. The discharge of the remaining 30 neurons was produced directly by weak stimulation of the ipsilateral vestibular nerve. Elicited spikes follow each stimulus, but the latent periods are variable and therefore their response is similar to that of Type I neurons to ipsilateral stimulation of the vestibular nerve. With rhythmic stimulation having an interval of less than 5 msec, the frequency of elicited discharges does not reproduce the frequency of stimulation. These results show that Type II responses were post-synaptic, and none of them appeared as a pre-synaptic potential of the action of primary afferent fibers. It is also improbable that Type II neurons are efferent fibers to the terminal organ.

Excitation thresholds of the examined Type II neurons with stimulation of the contralateral vestibular nerve fluctuated from 1.5 to 3 threshold values of the potential N_1. These values were higher than the intensity necessary for the excitation of such Type II neurons, which were influenced only by stimulation of the contralateral labyrinth nerve. It is possible that several of these contralateral exciting effects, in particular those obtained with stimulation 2-3 times greater than the threshold of the potential N_1, were elicited by general activation of the underlying reticular formation and were not connected with a specific function of the commissural fibers. In general, ipsilaterally activating Type II neurons have weak connections with the commissural fibers, while Type II neurons which are insignificantly activating ipsilaterally receive strong exciting influences through the commissural fibers.

The following facts attest to the fact that several Type II neurons, which were less subject to commissural influences and are activated by a single stimulus of the ipsilateral nerve, receive an inhibitory influence from the ipsilateral semicircular canal. Thus, after unilateral labyrinth destruction, Type II responses were registered even from the neurons of the vestibular nuclei on the intact side. The probability of registering Type II neurons on the intact side was sufficiently low, evidently due to the removal of the exciting influences from the contralateral

labyrinth leading to a Type II response. Under the given experimental conditions, a single sensory impulse related to rotation can originate from the ipsilateral horizontal canal. Insofar as the /124
terminal organ of the horizontal canal indicates only a Type I response (Groen, Lowenstein, Vendric, 1952), the discharge frequencies of the Type II neurons decrease together with an increase in the activity of the primary afferents from the horizontal canal. It appears to be possible that at least several of the vestibular neurons are inhibited by the ipsilateral horizontal canal, thus giving a Type II response (the mechanism of this inhibition is unclear at the present time). For the excitation of such neurons, the intensity of stimulation of the contralateral vestibular nerve is necessary 2.5 - 3 times greater than the threshold of the potential N_1. This intensity of stimulation is stronger than that necessary for excitation of the commissural system.

Spike amplitudes of many ipsilaterally exciting Type II neurons were sufficiently greater (usually 300 - 1200 μV), i.e., of such a magnitude as amplitudes of Type I neurons. Localization of the neurons was not limited to the ventral portion of the vestibular nuclei; apparently they were scattered over various portions of the vestibular nuclei, although systematic investigations of the localization of these neurons were not conducted by Shimazu and Precht.

Histological investigations showed that the neurons of the vestibular nuclei send commissural fibers to the contralateral vestibular nuclei. These fibers are distributed in the contralateral region (Gray, 1926), on the ventral border of the medial nucleus (Ferrara et al., 1940), in the medial half of the lateral nucleus (Gray, 1926; A. Rasmussen, 1932) and in the descending nucleus (Gray, 1926, Ferraro et al., 1940). No definite conclusions are drawn concerning the superior nucleus (Gray, 1926). Commissural fibers intersect the medial line of the brain stem under the bottom of the fourth ventricle (Gray, 1926; A. Rasmussen, 1932; Ferraro et al., 1940). With these anatomical data the paths conducting these potentials (Shimazu, Precht, 1966) are in good agreement with the distribution in the contralateral vestibular nuclei of summary potentials elicted by a single electrical stimulation of the vestibular nerve.

Mickle and Ades (1954) could not register any elicited activity in the contralateral vestibular nuclei of animals anaesthetized with nembutal. Gernandt et al. (1959) also did not discover a significant elicited response in the contralateral vestibular nuclei even with the decerebration of an animal (cat). In contrast to these negative results, Shimazu and Precht (1966), in the research under consideration, showed that contralateral elicited potentials, although small in size, were essential and were discovered only in a limited region of the vestibular nuclei. It is also necessary to note that trans-synaptic activity of the vestibular neuron was very sensitive to the physiological condition of the animal and to nembutal anaesthesia (de Vito et al, 1956; Precht, Shimazu, 1965).

Two peaks of the elicited contralateral positive potential /125
(Fig. 36A, c) with respective latent periods of 2.5 and 4 msec could reflect the potentials N_1 and N_2 of the stimulated side, insofar as the interval between N_1 and N_2 is around 1.5 msec which corresponds to the interval between the summits of the two positive peaks. Analogously, it might be possible to explain the components of the negative summary potentials of commissural fibers (Fig. 36A, b). A prolongation of this complex potential on the order of 5-6 msec is much greater than the prolongation of potentials registered in a monosynaptic path (Brooks, Eccles, 1947; Precht, Shimazu, 1965). Probably this is connected with the presence of a broad band of latent periods of tonic vestibular units, activated on the stimulated side (Precht, Shimazu, 1965), which in turn leads to temporal dispersion of impulses conducted along the commissural fibers. The amplitude of contralateral positive potentials (50-70 μV) is much less than the amplitude of the potential P (300-400 μV), reflecting electrical response of the primary afferents, which can be explained by the relatively small number of commissural fibers as well as by the temporal dispersion of the intersecting impulses.

Contralateral inhibition of several vestibular neurons was first described by de Vito et al. (1956) with stimulation of the labyrinth by polarization. They also discovered that other neurons were excited by such stimulation, although they belonged to Deiter's nucleus. In the experiments of Schimazu and Precht (1966) the registered neurons were intensified not only automatically but also physiologically with natural rotational stimulation connecting their responses with the excitation of the horizontal semicircular canal. After physiological identification, the results were completely definite; i.e., Type I neurons were inhibited and Type II neurons excited with stimulation of the contralateral vestibular nerve.

Shimazu and Precht (1966), in order to elicit inhibition of the contralateral Type I neurons, did not separately stimulate the branch of the vestibular nerve innervating the horizontal semicircular canal, insofar as they could not establish the absence of propagation of the stimulation current over the nerve fibers of other terminal labyrinth organs. However, impulses producing inhibition of the contralateral Type I neurons at least partially must originate from the horizontal canal, since the threshold of Type I neurons to ipsilateral angular acceleration was significantly raised after destruction of the contralateral labyrinth. In other words, cross-inhibiting influences from the intact semicircular canal can either be increased or diminished in response to horizontal angular acceleration, thus taking part in responses of the contralateral Type I neurons to rotational stimulation. This point /126
of view is also strengthened by the fact that Type I neurons, seldom found on the destroyed side of severely decerebrated animals, in comparison with chronic animals (cf. Chap. IV), were inhibited from the contralateral horizontal canal, showing a Type I response to rotational stimulation. This argument does not exclude the possibility of inhibitory influences of other terminal organs on the contralateral Type I neurons.

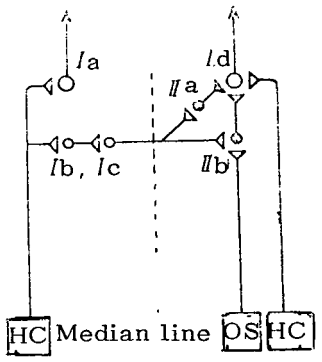

Fig. 39. Schematic Drawing of the Commissural Inhibitory Paths. I a, b, c, d: Type I Neurons; II a, b: Type II Neurons;HC - Horizontal Semicircular Canal; OS - Other Sections of the Vestibular Apparatus. Inhibitory Neurons are Indicated in Black (Shimazu, Precht, 1966).

In Figure 39 a schematic drawing is presented, proposed by Shimazu and Precht for the explanation of the neuromechanism of inhibition of Type I neurons and excitation of Type II neurons from the contralateral labyrinth. The shortest latent period of impulses conducted along the commissurae fibers is 2 - 2.1 msec after single stimulation of the vestibular nerve with registration from the central line of the dorsal portion of the brain stem. Insofar as the time of the conduction of impulses from the vestibular nuclei to the central line was 0.3 - 0.4 msec, the very first impulses must leave the vestibular nuclei of the stimulated side (left side, Fig. 39) 1.7 sec after stimulation. The latent period of a monosynaptically elicited potential N_1 in the ipsilateral vestibular nuclei equalled 1 msec after stimulation of the nerve (Precht, Shimazu, 1965). The value of the difference between these two latent periods (0.7 msec) could be explained by the presence of an intermediate synapsis. In Figure 39 these intercalary neurons, designated as Ib, excite the commissural neuron Ic. Neurons Ib and Ic, as well as the chief sensory neuron Ia, must show Type I responses. As Shimazu and Precht (1965) indicated, several of the tonic Type I neurons are not activated monosynaptically from the primary afferents even with strong stimulation. Some of them /127 might correspond to neuron Ic. It remained unclear whether the described commissural neuron is exclusively commissural or whether it sends collaterals of its ascending of descending axon to the contralateral vestibular nuclei.

The shortest latent period of excitation of Type II neurons from the contralateral labyrinth is 3.2 msec, i.e., it corresponds with the latent period of the subsequent negative summary potential (Fig. 36B,d) elicited by impulses conducted along the commissural fibers. The majority of such Type II neurons were localized in the ventral-medial portion of the vestibular nuclei, where negative summary potentials were more pronounced. These data lead to the conclusion that the subsequent negative summary potential in the contralateral vestibular nuclei is composed of the elicited potentials of activity of Type II neurons.

Spikes of Type II neurons appeared 0.7 msec after the arrival of impulses propagated along the commissural fibers. Insofar as the delay in the transmission through one synapse takes approximately 0.8 msec (Eccles, 1959), then it is completely probable that commissural fibers produced monosynaptic excitation of Type III neurons (IIa and IIb, Fib. 39).

Depression of spontaneous discharges of Type II neurons begins more than 4 msec after a single stimulation of the contralateral vestibular nerve, i.e., inhibitory processes lying at the basis of depression of spontaneous discharges are most highly developed within 5 sec after stimulation. As is possible the mechanism for the realization of this inhibition could be the presynaptic inhibition established in the central nervous system (Eccles, 1966) which is elicited by depolarization of the primary vestibular afferents. Spontaneous activity of Type I neurons is chiefly maintained by spontaneous impulsation of primary vestibular afferents. If these primary fibers are depolarized by means of commissural influences, the activity of Type I neurons could be consequently depressed. However such a means of depression evidently does not appear to be the only one in the experiments of Shimazu and Precht, (1966) since the cross-inhibitory influences can easily be discovered even in unilaterally chronic labyrinth ectomized animals (cf. Chapter IV), where Type I neurons were registered on the injured side. Under these conditions spontaneous activity of the vestibular nerve on the side of registration was completely removed, and consequently several other inhibitory mechanisms had to exist which differed from presynaptic inhibition produced by depolarization of primary afferents. Moreover, commissural inhibition begins extremely swiftly after 1.5 msec following the arrival of impulses originating from the contralateral side, and the entire process of inhibition begins within 30-40 msec. Such a temporal passage is much shorter than the presynaptic inhibition established in the spinal cord of mammals.

Another possible mechanism of inhibition might be the post- /128
synaptic inhibition accomplished by the commissural fibers. In this case the axon of several commissural neurons may have inhibitory synapses on their endings, acting on the contralateral Type I neurons, while other commissural fibers may be exciting for Type II neurons. However, contralateral elicited summary positive potentials reflecting presynaptic activity of the commissural fibers were localized in the ventral-medial portion of the vestibular nuclei, where the majority of Type II neurons which were excited by commissural fibers were discovered. On the other hand, Shimazu and Precht did not discover such summary potentials in the central or dorsal portions of the medial or superior nuclei where the majority of Type II neurons were localized. Presynaptic discharges producing inhibition of Type II neurons evidently are more dispersed in time than discharges of commissural fibers, probably due to intermediate synapsis which makes the potential less visible. A similar distribution of contralateral summary potential, different from the

arrangement of Type II neurons, decreases the probability of the existence of such a mechanism.

Finally, it is possible that post-synaptic inhibition is manifested through intercalary inhibitory neurons. If this is so, then it is possible to assume that several Type II neurons are intercalary inhibitory neurons (IIa, and IIb, Fig. 39) in the sense that they are activated with stimulation of the contralateral horizontal canal through commissural fibers and have inhibitory influences on the homolateral Type I neurons (Id). Such a mechanism is similar to the central path of inhibitory action on motoneurons of antagonistic muscles from afferents of group Ia (Eccles, et al., 1956). This hypothesis agrees well with the following results. On Type I and Type II neurons from one and the same side, the ipso- or the contralateral labyrinth always has reciprocal influences, and excitation of Type II neurons begins after 0.8 msec before inhibition of Type I neurons. Inhibition and excitation is manifested through the same path, the commissural fibers. The threshold for excitation of Type II neurons with stimulation of the contralateral vestibular nerve is lower than for inhibition of Type I neurons. This leads to the concept that for clear inhibition of Type I neuron the excitation of many Type II neurons is necessary. Commissure amplitudes of Type II neurons excited through a commissural fiber are definitely lower than the usual amplitudes of Type I neurons. This can be explained by the fact that Type II neurons are smaller in size than Type I neurons. Type II neurons often respond to a single stimulus of the contralateral vestibular nerve by high frequency /129
twin discharges. These repetitive discharges of Type II neurons can produce prolonged inhibition of Type I neurons up to 20-40 msec (Shimazu, Precht, 1965).

The localization of Type II neurons (IIa, Fig. 39), which are connected exclusively with the commissural function and are not excited ipsilaterally, evidently appears very important. These neurons are localized chiefly in the ventral portions of the medial nucleus and in central medial portions of the superior nucleus. According to Walberg and coll. (1958) the medial region and the ventral stria of the medial nucleus are free from terminal degeneration of primary vestibular afferents. In the superior nucleus, the peripheral zones are almost free from degeneration. Thus the localization of Type II neurons, which are not subject to the influence of the ipsilateral labyrinth, corresponds partially to the regions free from primary vestibular afferents. Insofar as Type II neurons localized in these regions play a paramount role in the function of the vestibular nuclei, these "nonvestibular" regions (Walberg, et al, 1958) must be viewed as vestibular, which corresponds to the assumption of Brodal and coll. (1966).

Several of the commissurally exciting Type II neurons were activated even monosynaptically from the ipsilaterally primary afferents. As was noted above, this ipsilateral influence can originate from the terminal organs, as differentiated from the hori-

zontal canal (for example, from the vertical canal). Thus the chief sensory neurons conducting impulsation from the horizontal canal to various portions of the central nervous system can be inhibited by several other terminal organs on the same side through inhibitory neurons. Inhibition of several Type II neurons by the ipsilateral horizontal canal can be of the same kind. Several observations of the influences of several labyrinth afferents on single vestibular neurons were conducted by Duensing and Schaefer (1959). The mechanism of such interaction, however, is far from being clear either in the peripheral or in the central sections of the vestibular system. The experiments of Shimazu and Precht (1966) give the possibility of assuming an inhibitory interaction inside the vestibular nuclei between the various labyrinth sensory systems of the same size. The possible function of this is to sharpen the input differences of vestibular impulsation connected with the motion of the head in space, which is true for various types of sensory systems (Katsuki et al., 1959; Hartline, Ratliff, 1956).

Figure 39 presents only the commissural inhibitory path including the corresponding actions and does not present the crossed reticular one, which evidently is diffusely exciting. Examining the /130 functional significance of the cross-inhibitory influences, we conclude that during ipsilateral angular acceleration the discharge frequency of Type I neurons increases, not only due to an increase in activity of the ipsilateral canal but also due to a decrease in the tonic cross-inhibition as a result of the decrease in the activity of the contralateral horizontal canal. In other words, removal of the inhibitory influence (disinhibition) from the contralateral side increases the excitability of Type I neurons.

During contralateral angular acceleration, on the other hand impulsation from the ipsilateral horizontal canal decreases and cross-inhibition is strengthened. These complimentary influences from the ipsi- and contralateral canal insure high sensitivity responses of Type I neurons.

Responses of Neurons of the Vestibular Nuclei to Inclinations and Alternating Linear Accelerations

The reaction of specific units of the vestibular nuclei in animals (cat) to inclinations and linear accelerations were first described by Egmond (1943). The majority of units registered by the author which reacted to inclinations possessed spontaneous activity.

With a lateral inclination on the ipsilateral side, the discharge frequency of many units increased, and with inclination on the contralateral side the frequency decreased or the discharge completely disappeared. These same units reacted even to inclination in the sagittal plane, in truth with significant angles of inclination. It is not surprising that this type of unit reacts both to linear lateral acceleration and to rotation in the horizontal plane when the axis of rotation does not pass through the animal's

head in the following way: with acceleration (rotation) on the ipsilateral side, the discharge frequency decreased; with acceleration on the contralateral side, it increased. Several units reacted both to forward-backward linear acceleration and to vertical acceleration.

Other units were more subject to inclinations in the sagittal plane and reacted to downward motion.

The author observed neurons silent at rest, and also the phenomenon of adaptation under prolonged (to 33 sec) maintenance of the animal's head in an inclined position. Cramer (1962), conducting investigations of this phenomena, discovered that the original sufficiently large response to inclination decreases exponentially after 15-30 sec since the remaining stable discharge insignificantly differs from the frequency of spontaneous discharge.

Rupert et al., (1962) separated the neurons of the vestibular nuclei reacting to inclinations according to the character of spontaneous impulsation: neurons with a correct rhythmicity; neurons with an incorrect rhythmicity, and neurons discharging with doublets. Experiments were conducted on cats whose cerebelli were not removed.

With similar experimental conditions, Hiebert and Fernandez /131
(1965), registering the activity of Deiter's nucleus, discovered that more deeply located cells discharged with doublets, triplets and small groups of impulses, while cells distributed closer to the dorsal surface of the brain stem discharged with single impulses. These types of activity were maintained even with increase or decrease in discharge frequency during slow changes in body position in the frontal or sagittal planes. The experiments of Hiebert and Fernandez (1965) once more affirmed the variety of responses of the vestibular nuclei neurons (caudal portion of Deiter's nucleus) through inclinations in the sagittal and frontal planes. Thus, neurons were found which reacted with a decrease in discharge frequency to a downward inclination of the head and return to the normal position, while others reacted with an increase in frequency to upward elevation and return; a third group did not react. Moreover, several neurons reacted to downward inclination by an increase in the frequency of rhythmicity; with return to a normal position, they curtail it. With elevation of the head they also curtail it, and with a return increase it. Neurons were found which reacted in the opposite way. The same variety of neuron responses was observed also for lateral inclinations.

The observations made by the authors with repeated inclinations of the head in sequence (down-return, up-return, and also right-return, left-return) are interesting. In approximately one third of the neurons, frequency responses were changed from the first to the following repetition, others showed precise reproduction of frequency changes to 3, 4 and even 7 repetitions.

Schoen (1957) with microelectrode removals of charge from the vestibular nuclei of bony fish, discovered a significant number of units giving a change in frequency of the ideal sinusoidal shape due to lateral inclinations. But units were found during frequency changes in the shape of an asymmetric sinusoid, whereby inclination toward the side of excitation led to a greater change in frequency than inclination toward the side of inhibition.

It was found that the number of neurons reacting by excitation to inclination toward the ipsilateral side is approximately the same as those reacting by inhibition (35:25).

Neurons which were silent at rest, whose activity also increased, and neurons whose activity could only be inhibited were also found. These are unidirectional neurons.

The enumerated types of neurons duplicate the character of /132 changes in activity of single nerve fibers (Lowenstein, Roberts, 1949). But Schoen also observed a small number of neurons reacting with increase in activity to inclinations toward both sides.

In this section of the chapter we will also present data obtained with registration of action potentials of separate vestibular nuclei neurons, in particular Deiter's nucleus at rest, and with passive movement of the animal in the vertical plane.

Experiments were conducted on 30 cats. A mixture of chloralose (4-50 mg/kg) and nembutal (15 mg/kg) introduced intra-abdominally was used as anaesthesia. The head of the animal was fixed in a head holder of a stereotaxic instrument, made in the workshop of the A. A. Bogomolets Institute of Physiology of the Academy of Sciences of the Ukrainian SSR.

For entrance to the brain stem in the occipital bone of the skull, preliminarily freed of skin and muscles, with the aid of a dental drill a trephination opening 15 x 15 mm in size was made, the cerebellum was found, and afterwards it was completely removed. The osseous hemorrhage was stopped by plastering the edges of the opening with wax and by suction of the cerebellum with a sponge of "spongostan".

Removal of potentials of neuron action was made intracellularly using glass microelectrodes with a tip thickness of 1-3 μ filled with a 3 M solution of KCl. The microelectrode was immersed to a depth of 1-4 mm, 2-6 mm lateral of the central line and 3 mm forward and back from the angle of the rhomboid fascia. The immersion of the electrode was accomplished with the aid of a hydraulic manipulator. In order to protect the microelectrode from vibrations arising from the motion of the stand and the removal of pulse and respiratory motions of the brain stem, the micromanipulator was fixed on the frame of the stereotaxic instrument, and after conduction of the microelectrodes at the surface of the brain, a thickly diluted agar-agar was poured into the trephined opening.

The location of the microelectrode tip was controlled histologically. For this the medulla oblongata, fixed in a solution of 10% neutral formalin, together with the electrodes present in it was carefully prepared, and the place of electrode entrance was defined with the naked eye. Afterwards sections with a thickness of 20-30 μ were made on a freezing microtome. Subsequent tinting with hemotoxaline, according to the Nissl and Campos method, gave a precise picture of the microelectrode canal.

Before the beginning of the experiment[4] the animal together with the frame of the stereotaxic instrument were fixed onto a rocking stand (Fig. 40). The recording apparatus was the same as in experiments described in Chapter I. After microelectrode detection of a neuron with a spontaneous rhythmicity the latter was registered during 10-15 sec. If the activity of the cell was constant, and /133

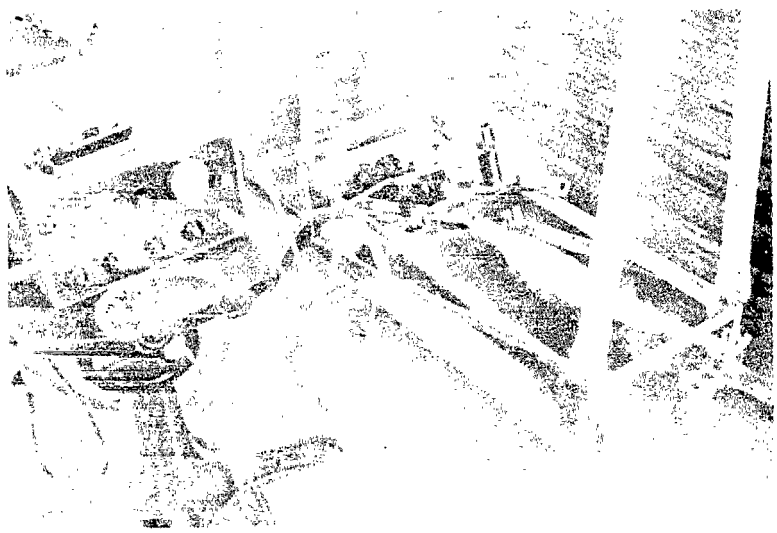

Fig. 40. Cat on a Rocking Stand

consequently was not connected with the mechanical action of the electrode on it, then the action potentials of this neuron were recorded during the same period (10-15 sec) against the background of vertical shifts and after the cessation. In a number of cases, background rhythmicity and its changes with rocking were conducted over 1-2 minutes. The reactions of neurons silent at rest to rocking were not studied.

According to the character of background rhythmic activity, neurons can be divided into three groups:

[4]Experiments were conducted with B. B. Yegorov. Yu. L. Limotskiy took part in the development of the method and part of the experiment.

(1) neurons with correct rhythmicity at a frequency of 5-50 imp/sec;
(2) neurons with a nerve rhythmicity, the action potential frequency of which fluctuated from 1-150 imp/sec;
(3) neurons with groups of impulses with specific periods of absence of activity.

Principally the same classification of neurons of vestibular nuclei according to the character of spontaneous activity were given by G. I. Gorgiladze (1966) and Fredrickson et al., (1966b).

Of 745 registered neurons, 84 did not change in rhythmicity with vertical motion of the animal.

In 439 neurons of 661 which reacted to shift in the body along /134 the vertical, an increase in rhythm frequency was observed independent of the direction of motion. In addition, neurons with the correct rhythmicity increased in frequency without noticeable perturbations of correct rhythm, and in neurons with a group background of rhythmicity, an increase in the number of action potentials in groups and a shortening of the intervals between the groups were discovered (Fig. 41).

Fig. 41. Neurons with Group Rhythmic Activity (a) At Rest; (b) With Rocking; (c) After Rocking.

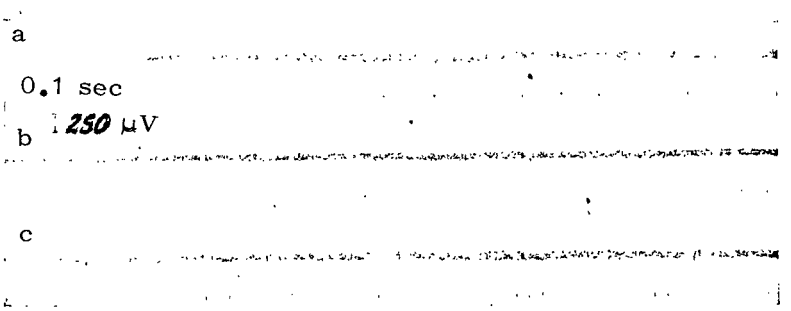

Fig. 42. Neuron With Incorrect Rhythmicity (a) At Rest; (b) With Rocking; (c) After Rocking.

120 neurons curtailed rhythmicity independent of the direction of motion of the stand. As is seen in Figure 42, a neuron with an

incorrect background rhythmicity generally stops impulse generation with vertical rocking.

Calculation of the number of action potentials of the neurons per 5 sec intervals on a B-2 apparatus, for example of 4 neurons (Fig. 43), demonstrates the change in rhythmicity during rocking. If after 5 seconds at rest the number of impulses fluctuated within the bounds of 30-40, then during rocking the number of impulses grew to 140-150 after 5 sec or sharply dropped until complete disappearance of activity. This figure also shows that with re- /135

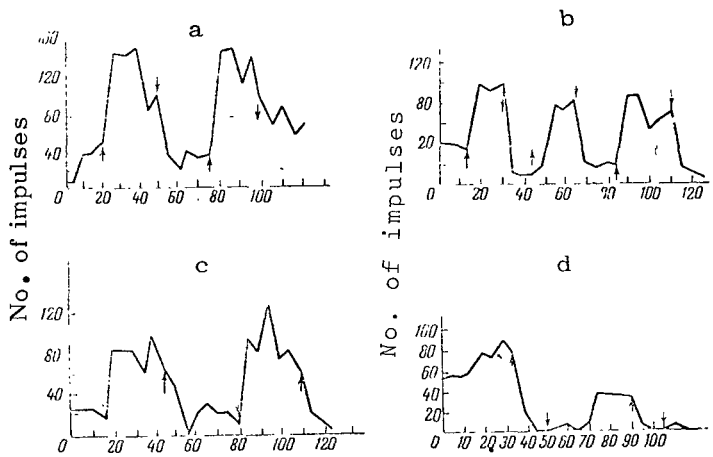

Fig. 43. Change in Impulsation Frequency of 4 Neurons (a,b,c and d) with Rocking. The Arrows Indicate the Beginning and End of the Rocking.

peated action (2-3 times) the character of the changes in background rhythmic activity was the same as during the first reaction.

The frequency of rhythmicity of 43 neurons increased with upward motion of the platform and restored the frequency of background rhythmicity with downward motion. Thirty-four neurons have the opposite characteristics: they increased in frequency of rhythmicity with downward motion and restored it with upward motion.

The rhythmicity of 25 neurons increased with upward motion and decreased with downward motion (Fig. 44).

After cessation of rocking, 50% (330) of the neurons restored their original rhythmicity during the registration time (15 sec). Composite data on the reactions of neurons during rocking are presented in Table 7.

There are no experiments analyzing the connections of the vestibular neuron reacting to linear accelerations, but in this relation the functional connections obtained in experiments with

polarization of the labyrinth by a constant current can be useful. Although a galvanic current is not an adequate stimulus for sensory organs, its action on the sensory epithelium, as Lowenstein showed (Lowensteim 1955), is algebraically added with electrical changes in the sensory epithelium produced by natural stimulation of terminal organs.

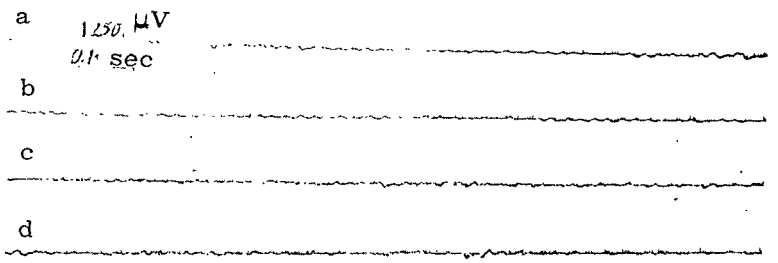

Fig. 44. A Neuron with Incorrect Rhythmicity (a) At Rest; (b) With Motion of the Platform Downwards; (c) With Motion of the Platform Upwards; (d) After Rocking. /136

Using polarization as a vestibular stimulus it is possible to simulate conditions near those obtained with adequate stimulations. According to the reactions of the neuron of the vestibular complex to labyrinth polarization it is impossible to reply to the question as to what terminal organs are connected to the neuron, since the terminal organs of the ampulla, utriculus, sacculus and cochlea are simultaneously stimulated. The possibility of neuron reaction to stimulation of terminal organs of the cochlea probably is excluded, since at the present time there is no anatomical proof that the cochlear fibers end in the vestibular nuclei. Moreover, acoustical stimulation does not influence neuron responses of the vestibular nuclei (Fredrickson et al, 1966b).

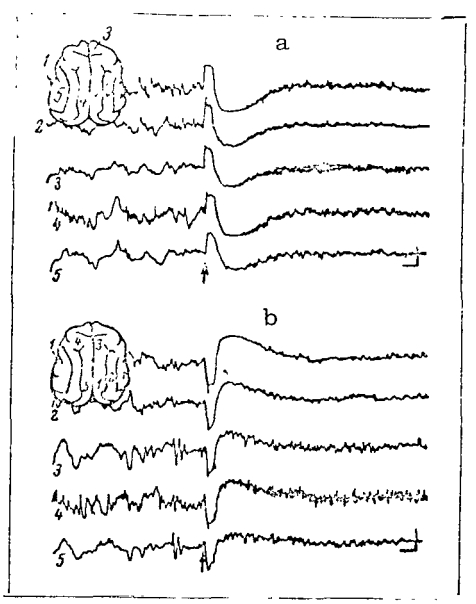

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Fig. 45. Influence of Polarization of the Labyrinth on EKG (A,B). (A,B) Polarization of the Right Labyrinth by Cathode (0.3 mA) and an Anode (0.45 mA). Calibration 300 μV; Scale of Time 250 msec. The Arrow Indicates the Moment of Inclusion of Positive Current to an EKOG Surge After Inclusion of Current (Artifact); (1-5) Removal from Points of the Cortex Designated by the Corresponding Figures on the Schematic Drawing (Gorgiladze, 1964).

TABLE 7. QUANTITATIVE DATA ON THE CHARACTER OF CHANGES IN RHYTHMICITY OF VARIOUS GROUPS OF NEURONS

Groups of Neurons	No. of Neurons	Increase in Frequency of Rhythmicity	Decrease in Frequency of Rhythmicity	Reaction With Motion of The Platform Upwards (Increase)	Reaction With Motion of The Platform Downwards (Increase)	Reaction With Motion of the Platform Upwards (Increase) and Downwards (Decrease)	Absence of Reaction
With Correct Rhythmicity	114	43	38	11	8	--	14
With Unequal Rhythmicity	537	344	70	20	13	20	70
With Groups of Potentials of Activity	94	52	12	12	13	5	--

Thus the conclusions obtained in experiments with polarization may be related to any terminal organs of the nonauditory labyrinth to an equal degree.

G. I. Gorgiladze and V. M. Federov (1964), in experiments on nonanaesthetized cats immobilized by means of flaxedil, showed that polarization of the labyrinth by means of a constant current of 0.08 - 0.1 mA elicits the characteristic changes on an electrocortiogram (EKOG) which are expressed by the appearance of high frequency, low amplitude waves, i.e., an electrographic "waking" begins. The effect is produced independent of whether a cathode or an anode is applied to the labyrinth (Fig. 45), although it is known that electrical activity of the 8th nerve is strengthened with the action of the cathode and suppressed by an anode (Khechinashvili, 1958).

With polarization of both labyrinths by a current of different direction, the activation reaction of EKOG is more strongly pronounced than with polarization of only one labyrinth by means of the same force. If both labyrinths are polarized by a current of one direction, no EKOG changes are observed. The absence of changes on an EKOG due to cathode polarization of both labyrinths attests

to the fact that a block of vestibular afferentation takes place in definite structures of the central nervous system.

G. I. Gorgiladze (1964, 1966b) proved that this block takes place in the vestibular nuclei themselves. Experiments were conducted on cats. Under the experimental conditions the flow of "Outside impulses" to the vestibular nuclei was severely limited. /138 Deep nembutal anaesthesia (60-80 mg/kg) eliminated influences from the side of the reticular formation and other central nervous organizations. Impulsation from the cerebellum was absent due to its removal. Impulses from the proprioceptors of the muscles were weakened due to curarization of the animal. Deep anaesthesia and the severe fixation of the head probably somewhat lowered even the afferent impulsations from the receptors.

Thus there was a somewhat simplified model of the vestibular nuclei where spontaneous activity was maintained chiefly by a constant impulsation from the vestibular receptor.

Cathode polarization of the ipsilateral labyrinth strengthened the activity of the majority of neurons; anode polarization suppressed it. Polarization of the contralateral labyrinth had the reverse effect: the cathode suppressed activity of the neurons and the anode strengthened it. Thus, changes in activity of the right and left vestibular nuclei with polarization of one labyrinth were reciprocal: excitation of the nuclei on one side was connected with inhibition of the nuclei on the other side.

Upon transmission of the current through both labyrinths simultaneously, the character of reaction depended on whether the current was imparted to both labyrinths in different or identical directions. If the cathode was applied to the ipsilateral labyrinth and the anode to the contralateral, then the neuron shows a much stronger activation than in the case of separate stimulation of the labyrinth. With reverse direction of current the neuron was suppressed much more strongly than with cathode stimulation of only the contralateral labyrinth; in addition opposite changes were observed in the nuclei of the opposite side. With polarization of both labyrinths by means of currents identical in strength and direction, spontaneous neuron activity of both the right and left vestibular nuclei were equally suppressed. Thus the activation reaction of an EKOG begins each time with the destruction of equilibrium between the right and left vestibular nuclei. The absence of reaction with simultaneous destruction of both labyrinths by currents of equal strength and of the same direction was caused by impulse blocking in both vestibular nuclei.

G. I. Gorgiladze assumes that suppression of the vestibular neuron activity in response to polarization of the contralateral labyrinth takes place by means of the activation of intercalary inhibitory neurons with short axons connected with the commissural neurons of the opposite side (Fig. 46). Insofar as receptors of the vestibular apparatus possess constant spontaneous activity,

this inhibitory neuron also must be constantly active and have an inhibitory influence on the vestibular neurons on the opposite side, thereby balancing the activity of the vestibular nuclei neurons on both sides.

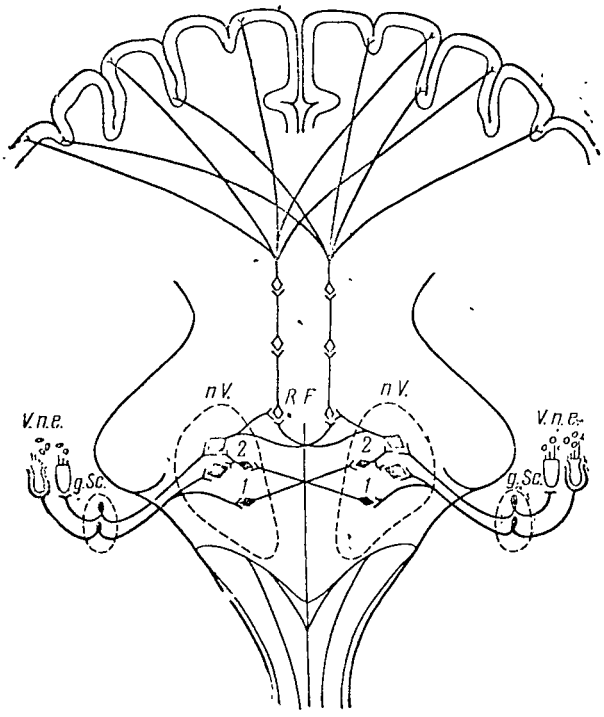

Fig. 46. Schematic Drawing of the Paired Work of the Vestibular Apparatus. V.n.e.- Vestibular Neuroepithelium; g. Sc. - Scarpa Ganglion; n.V. - Vestibular Nuclei; R.F. - Reticular Formation of the Medulla Oblongata; 1. Commissural Neurons; 2. Inhibitory Neurons (Gorgiladze, 1964). /139

But this same path with vestibular stimulation will make possible the destruction of equilibrium, insofar as the stronger the afferentation from one labyrinth the more active this inhibitory neuron, and the symmetrical side will be more suppressed. This inhibitory path evidently is very effective, since cathode stimulation of the contralateral labyrinth can completely suppress strong activation of the neuron in response to the same polarization of the ipsilateral labyrinth. The existence of inhibitory neurons makes it possible to explain the strengthening /140 of spontaneous activity in response to anode polarization of the contralateral labyrinth. Due to the suppression of spontaneous afferent impulsation by the anode, the inhibitory path will not function and naturally its constant inhibitory influence on the neurons of the contralateral nuclei will be removed, which leads to the appearance of neuron activity.

Some of the neurons of the vestibular nuclei (12%) recorded by the author reacted to the contralateral cathode by strengthening activity and to the contralateral anode by suppressing it. However these neurons did not react to ipsilateral polarization. Therefore it is possible that they appear only as inhibitory neurons.

The system proposed by G. I. Gorg'iladze is similar to the system of the functioning of the vestibular nuclei neurons reacting

to accelerated rotation (Fig. 39). Insofar as with polarization of the labyrinth even neurons connected with the receptor apparatus of the otolith organs are activated (or suppressed), then it is fully probable that there are also reciprocal relationships between the neurons reacting to inclinations.

But, on the other hand, labyrinths can function in all probability even synergically (Magnus, 1962; Szentagothai, 1967 et al.).

The vestibular nuclei, i.e., the first relay station on the path for the conduction of vestibular impulses, have been sufficiently well studied both morphologically and electrophysiologically at the present time.

In relation to their anatomical organization, the vestibular nuclei are exceptionally complex. Each of the four vestibular nuclei have their own individuality, both in cytoarchitectonics and in their afferent and efferent connections.

The difference between them in relation to architectonics and connections do not exclude numerous anatomical possibilities for interaction between the various groups of cells. It is hardly possible at the present time to assert that in the vestibular nuclei there are nurons reacting only to linear accelerations and only to angular ones, insofar as on the same neurons of the vestibular nuclei convergence of impulses from various sections of the vestibular apparatus takes place.

Normally between vestibular nuclei of both sides a dynamic balance exists. This balance is destroyed independently of whether afferent impulsation from one labyrinth is strengthened or suppressed.

There are at least three mechanisms which make possible great destruction of this equilibrium (Gorgiladze, 1966), elevating the sensitivity of the vestibular nuclei through afferent impulsation: the very anatomical distribution of both labyrinths in the temporal bone is such that with vestibular stimulations, impulsation from one labyrinth is strengthened and from the other is suppressed /141
(destruction of equilibrium takes place first at the periphery); the entrance into the vestibular nuclei, on the one hand, of strengthened impulsation, and on the other, an absence or decrease in afferent impulsation due to the existence of inhibitory neurons included between the right and left vestibular nuclei destroys this equilibrium still more; the existence of a third mechanism in the form of centrifugal fibers of the vestibular nerve will contribute to this destruction. Thus between the right and left vestibular nuclei there are reciprocal relationships.

CHAPTER IV

THE VESTIBULO-OCULOMOTOR REFLECTOR ARC

Structure of the Oculomotor Apparatus (OMA) Morphology

The oculomotor apparatus includes the external ocular muscles /142
(6 for each eye) the cranial cerebral nerves innervating these muscles (III, IV and VI), the oculomotor centers (nuclei of the enumerated nerves and the portions of the midbrain connected with them, the cerebellum and the higher oculomotor, i.e., frontal, occipital and several other cortical centers) and also special conducting paths, among which we note the medial longitudinal bundle, uniting the oculomotor centers with each other and with the nuclei located below; in particular, with the vestibular nuclei.

The general scheme of the OMA is given in Figure 47, but the sensory nerve fibers from particular muscle receptors (proprioreceptors) are not shown.

The eyeball is brought into motion by 6 muscles of which there are 4 straight ones (superior, inferior, medial and lateral) and two oblique ones (superior and inferior).

The action of the straight muscles is simple: they pull the eyeball in their direction; the oblique muscles turn the eyeball: the superior directs it downward and outward, and the inferior upward and outward. The superior oblique muscle is innervated by the trochlear nerve (n. trochlearis), the rectus lateralis by the abducting nerve (n. abducens), the remaining four by the oculomotor nerve (n. oculomotorius).

Warwick, in recent years (1950, 1953a, b, c, 1954, 1955, 1964), conducted comprehensive investigations into the structural organization of the nuclei of the oculomotor nerves (primarily on monkeys) by the retrograde degeneration method. After unilateral intracranial section it was established that:

(1) n. trochlearis and n. abducens originate entirely from the /143
corresponding nuclei; all fibers of the first nerve intersect, and those of the second do not intersect; all cells of these nuclei are subject to degenerative changes and therefore they can be considered to be motoneurons;

(2) fibers of n. oculomotorius originate from large multipolar cells and also from average-sized cells of the caudal central nucleus. Around 1/6 of these nerve fibers intersect before leaving the midbrain; after unilateral neurotomy, degeneration is observed in 41, i.e., 45% of the cells; therefore in the nucleus nuc. oculomotorius there is not a sufficient quantity of intercalary neurons for the existence of even simple reciprocal innervation. It is possible to assert that the chief lateral and caudal central nuclei of nuc. oculomotorius are homogeneous groups of motoneurons. Cells of the nuclei nuc. oculomotorius, the fibers of which intersect, occupy 2/3 of the chief lateral nuclei in the region adjacent to the central suture. In the nucleus of the rear commissure (Darkshevich's nucleus), in cajal's interstitial nucleus, in the dorsal nucleus of the suture, in Frank's subbundle nucleus and in the nucleus nuc. abducens there was not retrograde degeneration.

The chief nuclear components of nuc. oculomotorius were: (1) a large bilateral cellular mass located immediately rostral of the nuc. trochlearis. In the rostral direction the dimensions of the nucleus are contracted due to the disappearance first of the intermediate, then of the ventral and finally of the dorsal divisions of the nucleus.

The dorsal and ventral masses are seen in the majority of vertebrates including primates. They are represented in the form of columns, the axis of which is parallel to the axis of the aqueduct. A

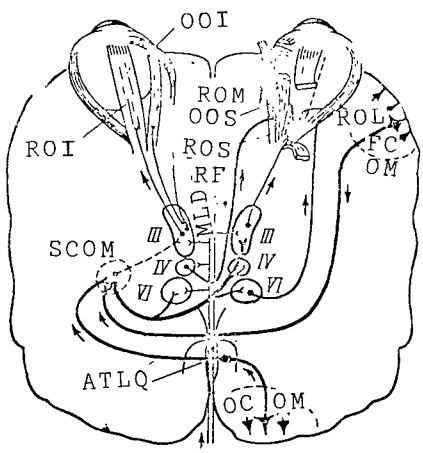

Fig. 47. General Scheme of the Oculomotor Apparatus (Seen Downwards). ROI - Rectus Oculi Inferior OOI - Obliqus Oculi Inferior, ROM - External Rectus Oculi Medialis, OOS - Obliquis Oculi Superior, ROS - Rectus Oculi Superior, ROL - External Rectus Oculi Lateralis, RF - Reticular Formation of the Brain Stem, MLD - Medial Longitudinal Bundle, SCOM - One of the Subcortical Centers of Ocular Movements, III, IV, VI - Occular Motor Nuclei and Corresponding Nerves, ATLQ - Anterior Tuber of the Lamina Quadrigemina, OCOM - Occipital Center of Ocular Movements, FCOM - Frontal Center of Ocular Movements (Matyushkin 1967a).

small group of cells is separated from the medial side of these main divisions of the nucleus and are variably represented near the central suture (paramedian group); (2) Bilaterally in a dorsal-medial /144 direction from the rostral half of the chief lateral nucleus is located Edinger-Westphal's nucleus; (3) in a rostral portion of the

nuclear complex, as Warwick assumes (1964), it is possible to separate only the forward central nucleus (well developed in monkeys) whose cells are similar to the cells of Edinger-Westpha's nucleus.

The central medial nucleus in monkeys is rudimentary and is found in 1/6 of cases; (4) in a caudal direction from the chief lateral nucleus is located the caudal central nucleus consisting of average-sized cells.

In the nucleic complex there is a clear tonic projection of the oculomotor muscles. The inferior rectus, inferior obliquus and medialis rectus muscles possess discrete motor groups of cells along the axis of the somatic nucleus in a dorsal-ventral direction. The superior rectus muscle is innervated by scattered neurons of the medial section in the caudal portion of the chief nucleus.

With the destruction of Dieter's nucleus, sufficiently powerful connections to the ipsilateral inferior rectus and obliquus muscles are found, since there is also a supplementary connection of the labyrinth to the ipsilateral inferior oculomotor muscles.

Two Motor Systems of the Oculomotor Apparatus of Higher Animals

D.P. Matyushkin (1961), in experiments on thalamic rabbits, registering the summary activity of the superior obliquus muscle of the eye with a needle electrode, discovered slow (with a period of more than 10 msec), constant fluctuations of one-phase potential of small amplitude (fractions of a microvolt). With threshold stimulation of the region of the fourth nerve nucleus by single right-angle stimulations (activity of 0.1 to 3. msec), the reaction of the ocular muscle (jerk) appeared on the electromyogram (EMG) in the form of a swift, two-phase potential of significant amplitude with a duration of up to 3 msec and a short latent period (1.5 - 2.0 msec). With strong stimulation the EMG showed two waves: a swift, two-phase oscillation and a subsequent slow, one-phase oscillation with a latent period of around 5 msec, in temporal parameters close to the background oscillations of the potential, but exceeding them in amplitude.

Intercellular removals of the potentials of separate muscle fibers showed that some fibers lack tonic activity. With electrical stimulation of the nucleus (Fig. 48a) these units gave high (to 60-90 mV), swift, single action potentials (with a period of 1.3 to 2.5 msec) characteristic for nontonic (phase) muscle fibers of the higher vertebrates (Shamarina, 1964). The latent period of these reactions was small (2-4 msec).

Other units (Fig. 48b) constantly gave rise to oscillations of /145 electrical potentials of comparatively low amplitude (12-28 mV) strongly expanding in time (with a period of more than 20 sec). In shape they correspond to oscillations of potentials described for

tonic muscle fibers in amphibians (Kuffler, Williams, 1953 a, b). The rhythm of oscillations of potentials of these oculomotor units in a rabbit would be more or less correct, and was within the limits

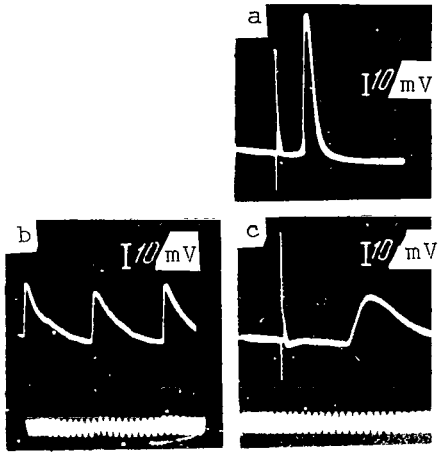

Fig. 48. Electromyograms of Phase (a) and Tonic (b,c) Fibers. (a,c) Responses of Fibers to Stimulation of the Trochlea Nerve Nucleus. Time Notation 200 Hz; (b) Constant Rhythmic Activity of a Tonic Unit. Time Notation 500 Hz (Matyushkin 1961).

of 20-75 Hz. Sometimes a superposition of potentials was observed (their summation) which is characteristic for tonic units (Kuffler, Williams, 1953 a,b). The tonic unit responded to stimulation of the fourth nerve nucleus by the same slow and weak oscillation of potentials. Reaction thresholds of these units were higher than the potential thresholds of phase unit reactions, and the latent period of response totaled 3-6 msec, i.e., greater than the reaction of type I fibers. Temporal parameters (prolongation of the peak, prolongation of the growth phase, half-value period) of action potentials of the ocular muscle phase fibers in a rabbit and of swift, two-phase potentials of its summary EMG corresponded to one another. The same proves to be correct for action potentials of tonic fibers and of slow, one-phase potentials of a summary EMG.

Thus the fast and slow potentials of summary EMG reflect the activity of phase and tonic muscle units. The two-phase nature of fast oscillations attests to the ability of phase fibers to conduct excitation, and the one-phase nature of slow fibers to their inability to conduct excitation of tonic fibers reflects the local character of the excitory process. In this regard, the tonic fibers of the ocular muscle in a rabbit are similar to the tonic fibers /146 of muscles in a frog (Zhudov, 1956), and also to the intrafusal muscle fibers of mamallian skeletal muscles (Granit, 1957).

Having examined the characteristics of excitability of motoneurons of the trochlear nerve nucleus innervating the phase muscle fibers and also the conduction speeds of these motor neurons in the neurites and the duration of neuromuscular transmission of the superior obliquus muscle in the eye of the rabbit, the author (Matyushkin 1962a) draws the conclusion that phase motor neurons of the trochlear nerve nucleus are typical alpha-motor neurons, possessing a high excitability and speed of conduction along the neurites (on the order of 80 m/sec). The action potentials of separate phase muscle fiber exciting intracellularly were indicators of the reactions of separate phase motor neurons to stimuli applied to the

nucleus. The swift (two-phase or even multiphase) action potential in the EMG of the muscle was an indicator of the summary reaction of these motor neurons. The ocular muscle tonic motor neurons in the rabbit are typical gamma-motor neurons, the neurites of which have a diameter of around 5 μ, relatively low excitability and speed of conduction of excitation around 30 m/sec (Matyushkin 1926b). It was found (Matyushkin, 1963a) that in the superior obliquus muscle of rabbit eyes there are two groups of tonic fibers, i.e., slower (half-value period 2.3 - 3.0 msec) and faster (4 - 6.5 msec). It is necessary to note that in the skeletal musculature of mammals among the intraspindular muscle fibers "of tonic type", having gamma-innervation, two groups were also found which differed in their character of response to nerve impulse (Boyd, 1959). Action potentials of tonic muscular fibers were used as an indicator of the activity of tonic multineurons, which potentials arise in response to stimulation in the region of the trochlear nerve nucleus. The data of D.P. Matyushkin's study (1952b) testified to the presence of multiple motor innervation of the ocular muscle tonic fibers. Such a type of innervation for muscle fibers, lacking conductability, is biologically justified since it ensures a contractive function to these fibers along their entire length. Examples of similar multiple innervation were given in earlier literature for tonic muscle systems of amphibians (Kuffler, 1955) for intrafusal muscle fibers (Hunt, Kuffler, 1951).

The neuro-muscular transmission in the ocular muscle's tonic system in a rabbit according to data obtained by the author, is manifested according to the following principle: one excitation potential in the muscle per nerve impulse. The neuromuscular transmission in the tonic system is significantly (4-5 times) slower in the phase system.

Continuing his investigations, Matyushkin (1963b) showed that the contraction reactions of the external ocular muscles to stimulation of corresponding nerves in rabbits and cats have phase and tonic components defining the work of phase and tonic units, which the nature of the corresponding electromyograms shows. As a rule, the tonic contraction component is masked by the phase component. /147
The phase component of the contraction reaction (excitation of phase units) can be eliminated by means of blocking the corresponding nerve in pulses by an anode of discharging current. In this case purely tonic reactions were recorded, i.e., slow and relative by weak contractions (in EMG, slow, one-phase oscillations of potentials). The temporal and force characteristics, obtained by the author, of contraction reactions in the phase and tonic systems of the oculomotor apparatus in mammals permit one to conclude that the phase system must ensure swift and significant eyeball movement and the tonic system ensuring slow, small movement and fixation. The scheme of the two motor systems of the OMA are shown on Figure 49.

What is the participation of the two motor systems of the oculomotor apparatus in labyrinth reflexes?

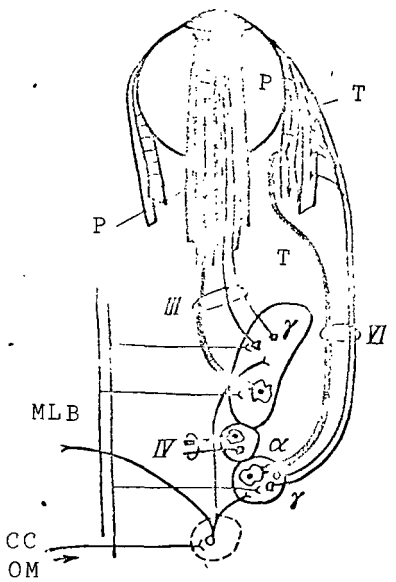

Fig. 49. Scheme of Two Motor Systems of the Oculomotor Apparatus. P - Phase (Swift) Muscle Fiber; T - Tonic (Slow) Muscle Fiber; III, IV and VI - Oculomotor Nuclei and Nerves; α - Alpha Motor Neurons (Large and Swift), γ - Gamma Motor Neurons (Small and Slow); MLB - Medial Longitudinal Bundle; CCOM - Paths from the Cortical Centers of Ocular Movements (Matyushkin 1967a).

P.I. Baychenko, D.P. Matyushkin and V.V. Suvorov (1967) investigated the labyrinth reflex on the left superior rectus muscle in rabbits placed in isometric work conditions. With a "crown upward" position of the /148 animals head, the superior rectus muscle was characterized by relatively low electrical activity. Upon turning the animal (fixed in a special rocking stand) around the longitudinal axis of the body in the direction of the registered muscle, the electrical activity of the latter increased. At the moment of turning, if the turning was made quickly (speed of 80-90 °/sec) the reflector reaction presented a significant strengthening of slow wave activity with the appearance of swift action potentials, i.e., it was manifested both by tonic and phase units.

With small turning speeds (3-25 °/sec) and with a stationary turning to one angle or another, the reaction emerges, as the authors showed, in the form of strengthened slow wave activity, increased in amplitude and frequency; i.e., this reaction is manifested only by the tonic system.

The strength of the described reaction, characterizing a growth in amplitude of the EMG, was in direct dependency upon the turning angle, which in the investigated band (to 85°) had an almost linear character.

Turning the animal in the direction opposite to the side of the investigated muscles led to suppression of the original tone of the latter (up to zero). This fact demonstrates the reciprocal inhibition of the given muscle's nerve centers under the conditions of activation of its antagonist.

The obtained data, first of all, attests to the fact that phase (swift) and tonic (slow) systems of the oculomotor apparatus par-

ticipate in different ways in the labyrinth reflex of the ocular muscles. As a rule, the phase system is drawn into the reaction only with strong and sharp stimulations of the labyrinth (of maculae and ampullas of the semicircular canals). The static labyrinth reflex basically is made by the tonic (slow) motor system.

The authors assume that the statoreceptors of the labyrinth have closer central connections with the gamma motor neurons of the tonic system than with the alpha motor neurons of the phase system.

Registering, with the aid of needle electrodes, the EMG of a prepared rectus oculi lateralis of a rabbit's eye with simultaneous recording of an electro-oculogram of the opposite eye with post-rotary nystagmus, Matyushkin (1967b) discovered that the swift phase of nystagmus[5] in the investigated muscle (as an antagonist) appears in the form of a relatively short "pack" of swift, two-phase action potentials, combining with a certain increase in strength of slow oscillation (primarily one-phase form). During the following slow phase in addition slow oscillations are registered, lower in ampli- /149
tude and frequency. When the investigated muscle operates as an antagonist the swift phase appeared as a more or less complete inhibition of electrical activity and the slow phase appeared as a gradual increase in amplitude in frequency of slow, one-phase oscillations of potentials (Fig. 50). Judging by the forms and temporal parameters, the swift, two-phase oscillations must be recognized as action potentials of the phase system muscle fibers, and the slow, single-phase oscillations as potentials of the tonic system fibers.

Thus the swift phase of nystagmus is accomplished by the joint operation of the phase and tonic systems (of muscle agonists). Such a double provision, in the opinion of D.P. Matyushkin, is completely justified: the phase system then lends speed to the given motion, and the tonic system ensures the maintenance of the attained position as well as the original one for the subsequent slow motion in the opposite direction.

The slow phase of nystagmus is accomplished by the tonic system of ocular muscles, the activity of which, in the agonist and the antagonist, change in the opposite way.

The data of D.P. Matyushkin's investigations (1967b) also testified to the fact that durations of swift phases of nystagmus-jumps (in contrast to the durations of the slow phases) do not have

[5] In the experiments the direction of nystagmus was defined by the swift phase. The investigated muscle was called an agonist by its active participation in the swift phase, and an antagonist by its active participation in the slow phase of nystagmus (of the opposite direction).

clear correlation with the durations of the nystagmic periods, and prove to be approximately constant for various strengths of phase

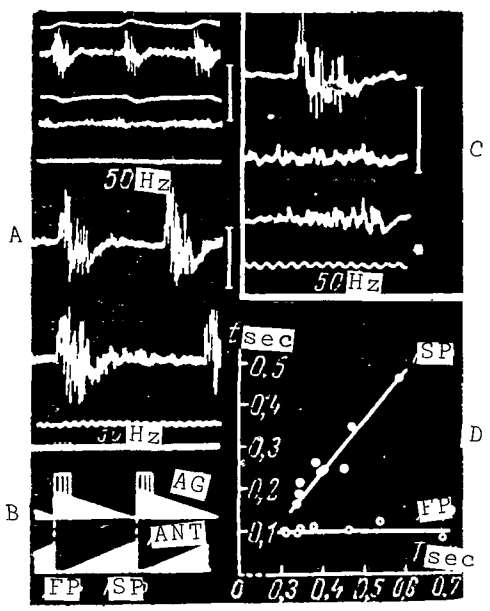

Fig. 50. Characteristics of Labyrinth Rotational Nystagmus (LRN). (A) EOG and EMG of the External Right Muscle in Swift Phases of Nystagmus; EOG and EMG of the Same Muscle in Slow Phases of Oppositely Directed Nystagmus. The Two Recordings of the Activity of the Muscle and Swift Phases of Nystagmus of Equal Frequency (Constancy of Duration of Two-Pnase Pulses PD); (B) Scheme of the Function of Phase (Shaded Area) and Tonic (White Area) Systems of the Muscle Agonist (AG) and the Muscle Antagonist (ANT) in the Fast (FP) and the Slow Phase (SP) LPN; (C) Forms of the EMG of Fast (Upper) and Slow (the 2 Lower) Recordings Without Nystagmus; (D) Dependency of Duration of SP and FP on the Duration of Nystagmus Periods (T); Calibration 1 mV (Matyushkin, 1967b).

pulses (jumps). In the opinion of the author, this fact indicates the existence of special mechanisms for limiting the duration of a jump (as a factor smearing the image on the retina and disturbing the vision).

A Model of Direction by the Oculomotor Apparatus

A study of the principles of OMA function is important for the /150 physiology of the nervous system and for the theory of direction. From this point of view the studies of the colleagues of the computer center of the Academy of Sciences of the Ukranian SSR (Petrov, Sragovich, Sushkov, 1966; Petrov, Sragovich, 1967; Bachelis, Sushkov, 1967) are interesting. In the studies a model of the OMA was developed as a single complex system accomplishing numerous functions.

The authors represent the directing system of the OMA as a finite automation, realized in the form of a combination of neuron structures stimulating the nervous system. We will examine below several of the ideas developed in these studies.

The Motor Complex. Movements of the eyeballs under the joint action of 6 muscles for each eye represent motions around immobile centers of the eyeballs and are described by two angles. We will examine the motions only in a horizontal plane, characterized by

one angle and realized by the muscles M_1, M_2, M_3, M_4 (Fig. 51). The muscles M_1 and M_4 turn the eyes outward toward the temples and M_2 and M_3 inward towards the nose. Corresponding with those presented above there are two types of muscle fibers: slow tonic and swift phase (T and P muscle fibers). They are innervated by nerve fibers (T and P nerve fibers) beginning, correspondingly in T and P neurons (TMN and PMN) of the motor nuclei N_1, N_2, N_3 and N_4. In Figure 51 the muscle fibers and nerve cells of the T and P systems are separated. Signaling the condition of the muscles comes from the proprioceptors connected with the T muscle fibers which are excited by special neurons of the nuclei. Feedback signals also come from tendinous receptors.

The combination of motor nuclei and innervating muscles forms a motor complex. It appears as the first level of OMA and the realization of motions ordered by the following higher levels of direction of the OMA enters its function. Motions accomplished by the first level are defined by two factors: (a) by the current condition of muscle fibers and neurons of the motor nuclei; (b) by the flow of signals arriving at the motor complex (afferent flow). The sources of the signals are very diverse: the vestibular apparatus (giving information on accelerations of the head and its position in space); the neck muscles (angles of rotation of the head relative to the body); the reticular formation (general diffuse action on the motor nuclei and support of muscle tone); the visual system, which is projected in a number of regions of the brain and has the primary influence, dominating the rest of the sources of the OMA. /151
All forms of activity can be divided into specific (connected with the provision of the visual functions of the oculomotor apparatus) and non-specific (the reticular formation for example appears to be their source). For a general description of the OMA, the authors unite all arriving signal flows in four centers (by the number of motor nuclei) and call them activators of the motor complex (AMC). The number of each of them corresponds with the number of the nucleus with which the activator is connected (Fig. 51). The direct action of the AMC on the motor complex is accomplished directly by the excitation of the key systems. Various stimulation of the nuclei of the motor complex causes contraction of the eye muscles which communicate to the eyeballs the various, sometimes oppositely directed, angular accelerations. In the absence of visual stimulus the activities of all AMC are weakly correlated and are non stationary in time.[6] Therefore T-muscle systems of each muscle function, within sufficiently broad bounds, almost independently of each other. As a result both eyes may wander irregularly without any agreement. The phase system does not participate in these motions.

The use of the abstract concept of the "activator of a motor

[6] Qualitatively the activity is defined by the number of simultaneously impulsing neurons and also by the frequencies of their impulsations.

complex" is useful because the correction of eye motions and the stabilization of their position through perturbations of various

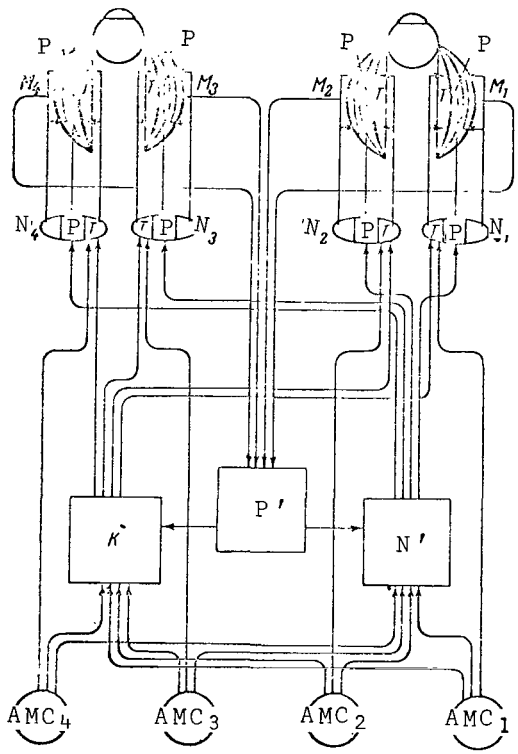

Fig. 51. Principal Scheme of the Model of the OMA (Petrov, Sragovich, 1967).

origins are established by a single principle, independent of the modalities of the perturbation. /152

The Coordinating and Stabilizing System of the OMA. The characteristic abilities of the lower level of the OMA are limited; it accomplishes eye motions and appears as a "slave" mechanism. It cannot assure coordinated eye motions with fluctuating signal currents in all four AMC's. As in other motor systems, this function is accomplished by a hierarchy of neuron structures, whereby the higher divisions act on the lower. The direction of the OMA by the motor complex is accomplished by the second level coordinating and stabilizing system of the OMA coordinating eye motions. The second level has two groups of inputs. Afferent flows arrive at the first group from the receptors of the muscles and tendons, and efferent flows arrive at the second from the AMC flowing through the branchings of the nerve trunks. This level performs its function by three mechanisms acting in parallel: (a) departure of the eye as a result of an increase of activity of one of the AMC's is partially compensated by proprioceptive connections entering the action (extension

reflex); (b) noticeable approach or divergence of the eyes (due to elevated activity of AMC 2 and 3 or AMC 1 and 4). These are compensated for by their slow departure or approach (convergence reflex); (c) simultaneous noticeable departure of both eyes in the same direction (due to elevated activity of AMC 1 and 3 or of AMC 2 and 4) compensated by a synchronic jump made by the F system in the opposite direction (in the nystagmoid reflex). The reflexes of extension and convergence are realized by T systems and in jumps the chief role belongs to F system. At the time of compensatory motions the T systems of the muscular antagonist (reciprocal inhibition) are suppressed.

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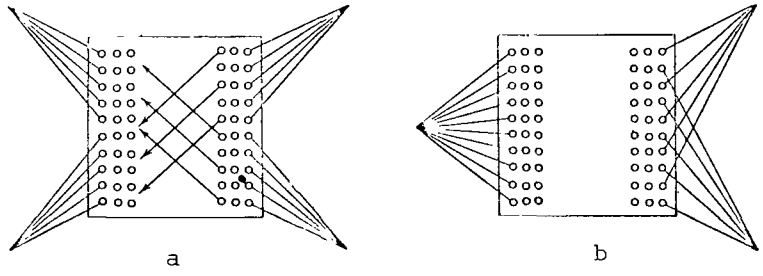

Fig. 52. Neuron Nets of the OMA. (a) Comparing; (b) Summarizing (Petrov, Sragovich, 1956).

Further we will limit ourselves describing the logic of the functioning of the second level, digressing from the localization, number and mutual distribution of its component structures. The developed model concepts are hypothetical. Only the proper experiments can answer the question of whether or not they are true or false. Figure 51 shows three structures, P, K and N, forming the second level of direction of the OMA. Structure P deals with the flow of proprioceptive information, realizes the expansion reflex and acts upon structures K and N ensuring, respectively, convergence and nystagmoid reflexes. Structure N realizes synchronic and equal abrupt motions of both eyes; comparing the activity of all AMC's, it developed a pair of AMC's, the elevated impulsation of which can draw both eyes to one side. For example, if AMC 1 and 3 exceed 2 and 4 in activity, the eyes must begin or have already begun to be diverted to the right. Having discovered this circumstance, structure N generates a volley of impulses entering the F system of muscle antagonists M_2 and M_4, simultaneously suppressing the key systems of contractive muscles M_1 and M_3. The condition of structure N is corrected by the proprioceptive afferentations entering it.

The structure K is intended for the realization of oppositely directed motions of the eyes: convergences and divergences. The activities of AMC's are also compared in it, and if it appears to be the base that the eyes must leave the central position (to con-

verge or separate), then excitation of the proper value is applied to the T systems of muscle antagonists. Actions from the N and K structures lead not only to eye motions but also change the conditions of muscle receptors, and consequently regulate the proprioceptive flow in structure P. Thus all components of the second level of the OMA appear to be mutuallv interactive.

Roughly, such are the concepts about the logic of the functioning of the second level of OMA directions.

The authors build structures of the second level of two neuron /154 nets accomplishing different functions. The first form of the nets is comparing. The comparing net consists of two subnets and has two groups of input neurons (Fig. 52a). Such nets compare the activity of bundles of fibers arriving at various groups of inputs. We will examine the structure and functioning of the subnet.

A subnet of a comparing net representsa multilayered neuron system. The nerve cells of the layer, following the input neurons, provide spatial and temporal summation of cell excitations of the preceding layers. Each neuron transmits excitation to many neurons of the following layers, but primarily to those lying nearby. Each neuron of the subnet receives excitation from many neurons of the preceding layers, especially those nearby. A weak or brief excitation enters the input neurons; it cannot pass through all the subnets and reach its output cells. It is possible to say that weak excitations will "stick" in the subnet. This takes place because its neurons are excited, if impulses from many preceding neurons arrive at them almost simultaneously. Strong excitations which arise at a sufficiently broad, compactly distributed set of input neurons passes through the subnet. The number of activating neurons passes through the subnet. The number of activating output neurons monotonously depends on the intensity of the input signal.

Both subjects of the comparing net are structured the same. Therefore weak excitations acting upon both groups of input neurons do not pass through the net. Even excitations which are almost equally strong on both subnets do not pass through it. The cause of such "locking" of the net is the interaction of the subnets: from active neurons of each half, inhibitory suppressing influences go to the other half. Actually a picture of the interaction can be presented in the following way: distributed in both subnets are intercalary neurons which begin to impulse when a excitation wave propagating in the subnet arrives at them. The axons of these neurons terminate in neurons of the other subnet and inhibit them (elevating the threshold of excitation). Their suppressing activities act on the other subnet, diffusely weakening its activity. Thus almost equally strong excitations of both subnets cannot reach the output neurons.

If excitations of various intensity go to a subnet for a certain time (to one-large, to another-small) when a strongly acting

subnet suppresses the weakly active one, it locks it and prevents it from having inhibitory influences on itself. According to the time lapse necessary for removal of obstacles on the part of the antagonistic subnet, the more active subnet allows the signal which has come to it to pass and its input neurons, having been excited, are discharged by a volley of impulses.

The second type of subnet is summarizing. It also consists /155
of a number of layers of neurons from which the input neurons receive impulsations from accumulated flows, as is shown in Figure 52b. Input neurons of one group of fibers are distributed alternately with input neurons of the other group. Neurons of the following layers are connected with many preceding neurons and, as usual, provide a spatial and temporal summation of excitation. The output of the summarizing net proves to be active, if both flows arriving at it are sufficiently intensive. In the opposite case this net does not let excitations pass.

We note one important characteristic of both types of nets: prolapse of a small number of the neurons comprising it does not change the transformation of input signals completed by them. Substantial destruction of the functions of the net comes with the exclusion of a significant number of neurons.

We will not examine the concrete means for constructing the structures of the second level of the OMA in models of visual afferentation, in questions of tonus regulation with the fixation of immobile points and change of points of fixation, etc., given by the authors (Petrov, Sragovich, 1967). We will deal only with a qualitative explanation of the appearance of nystagmus.

With a sufficiently swift rotation of the animal (vestibular test) impulsation from the labyrinth is strengthened. This signifies that a pair of activators (AMC 1 and 3 or AMC 2 and 4) excites the key systems of the corresponding nuclei and the eyes begin slow motion (right or left). Simultaneously signals from the vestibular apparatus enter structure N, and with the passage of time necessary for it to pass through its comparing nets (labyrinth period of the abrupt motion) it causes an abrupt motion to the opposite side (left or right).

Functional Connections of the OMA With the Vestibular Apparatus. Nerve Connections of the Vestibular Nuclei With Nuclei of the External Ocular Muscles

The facts established by Warwick (1950-1964) are very important from a clinical and physiological point of view, i.e., that: (1) the majority of motor neurons of a superior rectus muscle are localized in the rear portion of the main nucleus of the third nerve, whereby the roots to the muscle are intersecting; (2) motor neurons of the medial rectus muscle (roots do not intersect) are localized

in the median portion of the chief nucleus of the third nerve; and (3) neurons of the inferior rectus muscle, also with nonintersecting processes, are distributed in the forward portion of the chief nucleus of the third nerve.

Szentágothai (1964), investigating the distribution of fibers /156 degenerating after unilateral destruction of separate vestibular nuclei, discovered that injury to the superior vestibular nucleus (Bechterev's nucleus) caused primary degeneration in the dorsal-medial cellular group of the nuclei complex of the third nerve on the contralateral side at the level of the rear third of the nucleus. This portion of the nucleus provides the contralateral superior rectus muscle with fibers. Insofar as the primary vestibular neurons do not have intersecting fibers, two intersecting paths are possible: from the primary vestibular neurons of Bechterev's nucleus to the oculomotor nuclei, or intersection of the motor roots innervating the superior rectus muscle. Thus the labyrinth has a clearly localized anatomical projection to the ipsilateral superior rectus muscle. In the middle third of the nuclei complex of the nuc. oculomotorius, degeneration after destruction of Bechterev's nucleus was discovered ipsilaterally in the ventral portion which feeds the ipsilateral medial rectus muscle with fibers. The data obtained by Szentagothai are in agreement with the observations of Brodal et al. (1966) on the principal termination of the primary fibers of the vestibular nerve in the superior vestibular nucleus and the numerous connections of this nucleus with the mid-brain. It is somewhat strange that although degeneration in the contralateral nucleus (nuc. trochlearus) was discovered, it is less pronounced than degeneration in those portions of the nuclear complex of the nuc. oculomotorius which innervate the superior and medial rectus muscles. This fact, as Szentagothai assumes, can be explained only by the fact that the primary fibers terminate in various vestibular nuclei or by the fact that there may be separate paths for a pair of synergic muscles.

Injury to the rostral portion of the complex of the medial and descending vestibular nuclei led to degeneration of the nuc. trochlearis and also of the entire contralateral nuclei complex of the nuc. oculomotoris. It is especially important to emphasize that with the destruction of this nuclei complex, extensive degenerative changes were discovered in the forward and dorsal sections of the main nucleus of the third nerve. Neurons of these regions innervate primarily the ipsilateral inferior rectus and oblicuus muscles.

The ascending paths to the oculomotor nuclei from the lateral Deiter's nucleus appear to be important. In the case of incomplete destruction of this nucleus, degeneration in the ipsilateral nuc. trochlearis was discovered. It must be the case, considering the full intersection of the roots of the nuc. trochlearis, that there is a reflector connection with the contralateral superior obliquus muscle.

The connection between the labyrinth and the oculomotor muscles is provided both by complex (multineuron) paths and by synaptic /157
paths of the three neuron chains (if we exclude the receptor cells): (a) the primary vestibular neuron g. Scarpa; (b) the secondary vestibular neurons of the vestibular nuclei sending their fibers into the composition of the medial longitudinal bundle to the nuclei of the oculomotor nerve; and (c) motor neurons innervating the ocular musculature (Szentagothai, 1950; 1964; Szentagothai, 1967).

Nerve Connections of Specific Semicircular Canals With External Ocular Muscles.

With the aim of defining the nerve connection of each semicircular canal with the external ocular muscles, it is convenient to investigate the tonic deviations of the eye observed with definite conditions of electrical stimulations of the ampullar nerve (Cohen, Suzuki, 1963).

Cohen and others (Cohen et al., 1964a, c) and Suzuki and others (Suzuki et al., 1964) showed that with stimulation of the ampullar nerve of one forward semicircular canal, the resulting motion of the eye was nonconjugational: the ipsilateral eye moves upwards and the contralateral revolves (Fig. 53). These motions, in the first place, are accompanied by strong contractions of the ipsilateral superior rectus muscle and the contralateral inferior obliquus muscle. Weaker contraction is also observed in the ipsilateral superior obliquus and the contralateral superior rectus muscles. Thus the ipsilateral eye moves upwards with a small rotation, while in the contralateral one there is observed a slight motion upwards against a background of rotational motion.

Simultaneously, antagonists of each of the muscles included in the motion are weakened.

Stimulation of a horizontal canal nerve leads to conjugational contralateral horizontal motion of the eyes, during which the ipsilateral internal rectus and the contralateral external rectus muscles are strongly contracted.

Stimulation of the nerve of the rear vertical canal elicits rotational motion of the ipsilateral eye due to activation of the superior obliquus muscle, and to downward motion of the contralateral eye due to contraction of the inferior obliquus muscle. Simultaneously the ipsilateral inferior rectus and the contralateral obliquus muscles give weak downward directed and rotational components to the motion of the eyes.

Some activity appears even in the medial and the lateral rectus muscle during stimulation of the nerves of the forward or rear canals or in the inferior and superior rectus and obliquus muscles during stimulation of the horizontal canal.

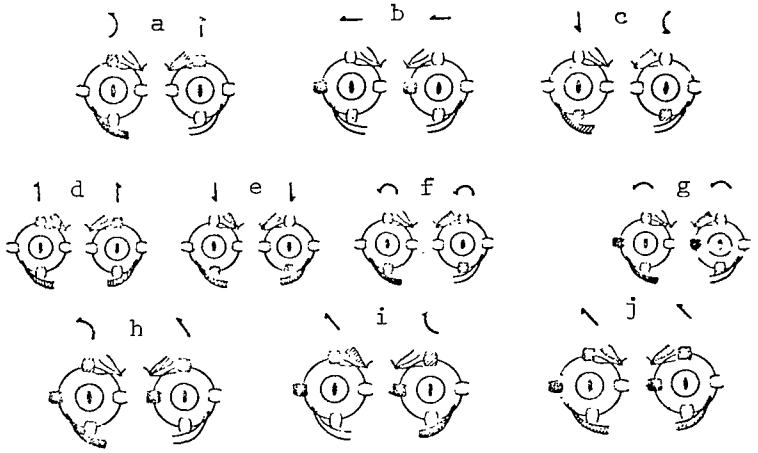

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Fig. 53. Motion of the Eyes with Stimulation of the Ampullar Nerves. (a) Stimulation of the Nerves of the Left Forward Canal; (b) Same of the Left Horizontal Canals; (c) Same of the Left Rear Canal; (d) Same of Both Forward Canals; (e) Same of Both Rear Canals; (f) Same of Left Forward and Rear Canals; (g) Same of the Left Forward Horizontal and Rear Canals; (h) Same of the Left Forward and Horizontal Canals; (i) Same of the Right Forward and Left Horizontal Canals; (j) Same of the Right Forward and Left Forward and Horizontal Canals. Strongly Contracting Muscles are in Black; Weakly Contracting Ones are Shaded; Noncontracting Muscles are White. (Cohen et al, 1964).

If the nerves of both forward vertical canals are stimulated, the motion of the eyes is straight upwards. Upward directed motion of each eye is stronger than with stimulation of the nerve of one canal, and rotational motion of the contralateral eye during stimulation of one canal disappears. Bilateral stimulation of both rear canals produces strong downward motion of the eyes; in addition, rotational motions also are absent and rotational downward motion is stronger than with stimulation of one rear canal. In contract to the vertical motions produced by stimulation of both forward and rear canals, combined stimulation of the ipsilateral forward and rear canals elicits conjugated rotational motion. In both eyes upwards and downward directed motions elicited by separate stimulation of the forward and rear canals, as well as rotational motion appear. Stimulation of all three canals on one side produces horizontal rotational motion of the eyeballs similar to that observed with peripheral destructions.

When one horizontal canal is stimulated simultaneously with the forward and rear canal, unconjugated oblique motions of the eyes are observed. Varying the intensity of the current impulses in packets of stimuli applied to either ampullar nerve, it is possible to change the angle of inclination of the resulting eye motion. /159

A single stimulation of both canals lying in one plane, i.e., of both horizontal canals or of one forward and contralateral rear canal, does not cause eye motion. In addition, recording of muscle strain generated in antagonists during stimulation is stronger and predominates over the excitation produced by these canals.

Observations conducted with electrical stimulation of the ampullar nerve illustrate the potential nerve connections which connect the semicircular canals with the eye muscles.

Although exciting nerve activity from the semicircular canals can be broadly distributed between the eye muscles with various experimental conditions (Lorento de No, 1932; Szentagothai, 1950) the data of Cohen et al. indicate that in intact animals there is a highly organized combination of excitation and inhibition processes which lead to conjugated horizontal eye motions when one horizontal canal is activated, and to dissociated motions with the motion of one eye in the vertical plane, or to rotation of the other when one forward or rear canal is stimulated.

The greater portion of the exciting connections discovered by the authors is similar to those found by Szentagothai (1950). However, the importance of the activation and inhibition of synergists, of principal eye muscles and of their antagonists cannot be traced, but it is necessary to understand the results of the combined stimulation of canals. For example, during stimulation of the left forward canal, the right and inferior obliquus muscles are strongly activated and the right superior obliquus is inhibited in order to produce rotational motion. When the right forward canal is stimulated, the right superior obliquus muscle is synergically activated and the right inferior obliquus is inhibited. If both forward canals are stimulated this activity is summarized; contractions in both the right superior and inferior obliquus muscles are blocked, and the right eye moves directly upwards without rotation. Similar but reversed events take place in the left eye in order to produce conjugated upward motion. On the other hand, if the forward and rear canals of one side are stimulated, contractions of the muscles producing fewer upward and downward motions are blocked (Fig. 53), and as a result conjugated rotational motion appears.

Motions elicited by electrical stimulation are similar to reflector motions of the eyes, which take place when the head turns, and also are similar to tonic divergences of the eyes elicited by caloric stimulation (Table 8 and 9). Direct stimulation of the ampullar nerve of the left horizontal canal elicits conjugated contralateral motion of the eyes to the right, which is similar to the motion of the eyes during rotation of the head to the left or with tonic divergences elicited by calarization by means of warm water of the left or cold water of the right ear when the head is deflected backwards by 60°. /160

Bilateral stimulation of the forward canals produces upward motion of the eyes which is similar to the motion of the eyes with rotation of the head downwards or bilateral warm calorization. Effects of stimulation of the rear canals are opposite and produce downward motions of the eyes, as with rotation of the head upwards or with bilateral calorization by means of cold water. Electrical stimulation simultaneously of the forward and rear canals of one side produces rotational motion of the eyes similar to the motion with rotation of the head in the frontal plane. The combined activation of the horizontal and rear canals on one side leads to oblique movement of the eyes with an angle of deflection from the horizontal depending on the correlation of intensities of canal stimulation which is similar to motions of the eyes during rotations of the head in the planes intermediate between frontal and sagittal.

TABLE 8 OCULOMOTOR RESPONSES WITH CALARIC (COLD AND WARM) STIMULATION OF THE LABYRINTHS OF INTACT MONKEYS (Cohen et al., 1964b)

Calaric stimulation	Stimulated Ear	Oculomotor response	
		Right constituent	Left constituent
Stimulation of one ear, body and head vertical			
Cold	Right	Tonic deflection to right	Nystagmus with swift component leftwards
Warm	The same	Nystagmus with swift components to the right	Tonic deflection to the left
Cold	Left	The same	The same
Warm	The same	Tonic deflection to the left	Nystagmus with swift component to the left
Simultaneous stimulation of both ears			
Warm	Bilateral	Nystagmus with swift component upward	Tonic deflection downward
Cold	The same	Tonic deflection upward	Nystagmus with swift component downward

The eye motions elicited by electric stimulation of a single canal are characteristic of a real canal. This characteristic response is neutralized or blocked when the canals of the opposite side lying in one plane are stimulated, since most of the eye is absent. This fact attests to the extremely fixed nature of the activities. Under natural conditions, a stimulus exciting the ampulla of one canal is usually accompanied by corresponding inhibition of the activity of the ampullar canal in the same plane but on the opposite side (Table 8). However, unilateral stimulation /161

TABLE 9 OCULOMOTOR RESPONSES AFTER ROTATIONAL STIMULATION OF A LABYRINTH OF INTACT MONKEYS (Cohen et al., 1964b)

Direction of Rotation	Oculomotor Response	
	Right Component	Left Component
Clockwise	Tonic deflection to right	Nystagmus with swift component to the left
Counter-clockwise	Nystagmus with swift component to the right	Tonic deflection to the left
	HEAD DOWNWARDS	
Clockwise	Rotational nystagmus with swift component to the right and counterclockwise	Tonic deflection clockwise and to the left
Counter-clockwise	Tonic deflection counterclockwise and to the right	Rotational nystagmus with swift component to the left and clockwise
	TO THE RIGHT SIDE	
Clockwise	Tonic deflection upward	Nystagmus with swift component downward
Counter-clockwise	Nystagmus with swift component upward	Tonic deflection downward
	TO THE LEFT SIDE	
Clockwise	Nystagmus with swift component upward	Tonic deflection downward
Counter-clockwise	Tonic deflection upward	Nystagmus with swift component downward

produces models of inhibitory and exciting activities elicited by each canal in the ocular muscles. These activities are regularly summed in order to produce eye motion, the direction and amplitude of which can change, varying the force of stimulation and the combination of stimulating canals. The obtained data indicated the nature of the control which the semicircular canals exert over the motion of the eyes in the natural state.

Reactions of the Neurons of the Nuc. Abducens to Adequate Stimulation of the Semicircular Canals

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The neurons of the abducting nerve of the cat (Precht et al,

1967a; experiments made on nonanaesthetized decerebrated and decerebellized animals) are divided into two types by their reactions to angular acceleration. Of 328 neurons reacting to angular acceleration in the horizontal plane registered by the authors, the discharge frequency of 257 increased with contralateral angular acceleration and decreased with ipsilateral angular acceleration (type II A neurons). The remaining neurons showed reactions of the opposite character, i.e., Type IA neurons.

Of 257 Type A neurons, 171 possessed spontaneous activity. With extended contralateral angular acceleration, the discharge frequency in the neurons smoothly increased, attained a maximum (often to 300 imp/sec) and then remained constant despite the continuing action of angular acceleration, thus indicating the absence of adaptation. In several neurons the smooth increase in frequency was periodically interupted by a sharp decrease, probably due to nystagmus arising from acceleration.

After reaching a constant angular speed of rotation, the discharge frequency smoothly dropped to the level of spontaneous activity. Mathematical analysis of experimental material indicated that, as in Type I neurons of the vestibular nuclei, the dependency of a maximum change in frequency upon the value of long-acting constant angular acceleration in the range of 0.2 to 10 $^{\circ}/sec^2$ is approximated by a logarithmic function [cf. Formula (2), Chapter III]. In addition, the value of the coefficient b in spontaneously active (tonic) and silent (phase) Type IIA motor neurons was equal to 64.2 ± 50.9 and 84.1 ± 45.7 respectively, and the value of the threshold was 0.50 ± 0.27. The difference between the values in both cases is statistically unverifiable, in contrast to the sharply differentiating coefficients of tonic and kinetic Type I neurons of the vestibular nuclei. It must be emphasized that the average angular accelerations for an increase in discharge frequency of the tonic and phase motor neurons is on the same order as for tonic vestibular Type I neurons: 0.65 ± 0.25 $^{\circ}/sec^2$ (cf. Chapter III), indicating the higher sensitivity to angular accelerations of silent motor neurons in comparison with silent Type I neurons of the vestibular nuclei.

The value of the coefficient b of Type IA neurons totalled 42.1 ± 25.5 and the mean value of threshold acceleration 1.3 ± 0.6 $^{\circ}/sec^2$, which is somewhat higher in comparison with thresholds of Type IIA neurons, and also with those of tonic vestibular Type IA neurons.

Type IIA neurons were excited antidromically with stimulation of the 6th nerve and were distributed, as electrophysiological and histological analysis showed, in the nuc. abducens. Type IA neurons never were excited antidromically and were distributed in the ventral portion of the nucleus. /163 Electrical stimulation of the contralateral eighth nerve (very seldom of the ipsilateral one) excited Type IIA neurons (the shortest latent period was 2.1 msec), and weak

ipsilateral stimulation inhibited their activity and excited Type IA neurons (the shortest latency was 3.1 msec). The authors have still not been able to establish whether Type IA neurons are inhibitory or excitory.

Thus under conditions of rest only tonic motor neurons are responsible for the tone of the lateral rectus muscles. During rotation the silent neurons are also activated, participating in the direction of eye motions. They do not significantly differ from the tonic motor neurons in the size of threshold acceleration and speed of change in discharge frequency, but the latent period of response of silent motor neurons to angular acceleration is always longer than that of tonic ones (Precht et al., 1967).

The Slow and Fast Components of Nystagmus

Stimulation of the peripheral sections of the vestibular system i.e., the semicircular canals, by calarization, polarization and rotation of the head, leads to precise and characteristic deviations of the eyes (Ewald, 1892; Magnus, 1962; Lorente de No, 1932; Lowenstein, Sand, 1940; Ledoux, 1958; Kornhuber, Fonseca, 1964 and many others). This deviation of the eye is periodically interrupted by a swift motion in the opposite direction leading to nystagmus.

Eye motions and nystagmus can also be elicited by electrical stimulation of the ampullar nerves of the semicircular canals (Fluur, 1959).

Cohen and Suzuki (1963) investigated the vestibular-oculomotor connections, observing motions of the eyes and the elicited electrical activity in eye muscles of cats and monkeys during various types of electrical stimulation of the ampullar nerve. A bipolar discharging electrode in these experiments was introduced between the bony and membranous walls of the labyrinth after opening the ampulla, so that the vestibulo-oculomotor paths were activated without direct involvement of the peripheral receptors. Action potentials of the ampullar nerve reproduced the stimulation up to a frequency of 250-300 impulses/sec. With frequencies higher than 300-400 impulses/sec, reproduction of the rhythm was incomplete.

Despite the fact that with single stimulation of the ampullar nerve a synchronized volley of impulses arrives in the vestibular nuclei, only a small portion of this activity reaches the eye muscles, syntactically connected with the vestibular nuclei (Fig. 54a, lower recording), the amplitude of elicited potential was insignificant and the latent period was 5-6 msec.

Stimulation by doubled current impulses, separated by a short /164
time interval, proved to be more effective in eliciting extraocular muscle potentials than a single stimulus, even if they were weaker in intensity than a single stimulus. Figure 54B shows that by decreasing the interval between two threshold stimuli from 75 to

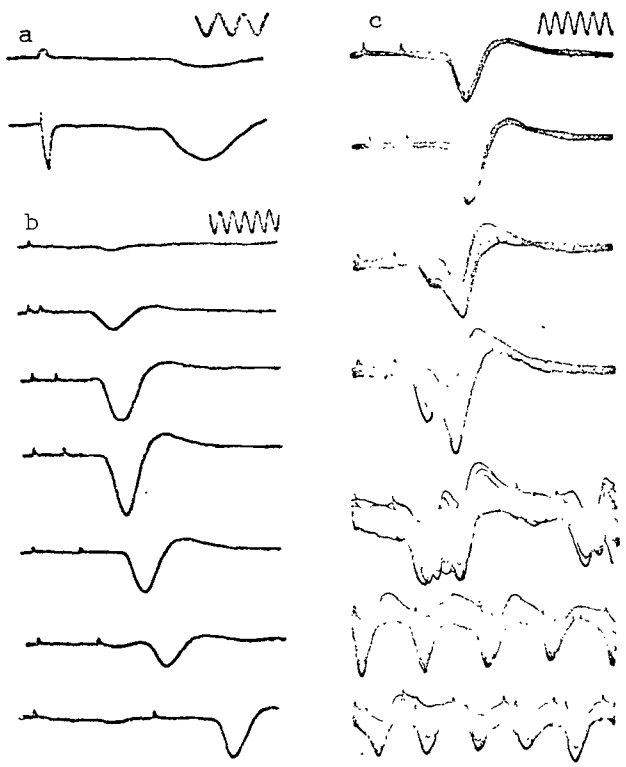

Fig. 54. Potentials of the Left Superior Rectus Muscle of a Cat's Eye With Stimulation by Right-Angle Electrical Impulses of the Ampullar Nerve of the Forward Semicircular Canal. (a) Stimulation by Single Impulses; (b) Stimulation by Paired Impulses; (c) Stimulation by Paired Impulses (Intervals Between Impulses 2.5 msec) at Frequencies of 1, 10, 20, 40, 77, 150 and 250 Pairs/second (Up-Down). Calibration 200 nV, Time Notation 1000 Hz (Cohen et al, 1964).

20 msec, the second stimulus produced a greater muscle potential; /165 moreover the latent period was shortened. With an interval between stimuli of 2.5 to 3 msec, the latent period of the elicited potential to the second stimulus was minimal (2.8 to 3 msec), and the amplitude was maximum (Fig. 54b, the fourth recording). Thus the first of the two stimuli facilitated the vestibulo-oculomotor paths for the second stimulus, which elicited a muscle potential of greater amplitude and with a shortened latent period. Paired stimuli elicited small eye motions.

Repetitive pair (group) stimuli with an interval between the stimuli of 2.5 to 3 msec elicited muscle potentials synchronically with each pair of stimuli up to a frequency of 250 pair/sec (Fig. 54b). With an increase in the strength of stimulus or in the number of stimuli in a group, the amplitude of the elicited eye motions increased. This motion consisted of a swift deviation to the side

from the mean position. When group discharge was ended, the eye slowly returned to the original position.

With a frequency of stimulation from 1 - 5 groups/sec, the eye motions were of a nystagmoid nature with a swift deviation from the middle position and with a slow return motion.

In contrast to the group stimuli, stimulation of the ampullar nerves by single impulses with frequency lower than 60 Hz, in general either did not elicit eye motions or led only to small deviations. With higher frequencies of stimulation the eyes slowly deviated from the central position in the direction of swift motions produced by stimulation in groups of impulses.

In fact, any addition of impulses to the ampullar nerve (in groups or in single repetitive stimulations in any combination which was effective for eliciting eye motions) always elicited an initial deviation of the eyes in the same direction for each real canal. So with stimulation of the ampullar nerve of the horizontal canal of monkeys, the eyes always began to move in a horizontal plane in the contralateral direction. This deviation often was short and was accompanied by swift motion of the eyes in the opposite direction. A swift return motion of the eyes was observed even with prolonged group stimuli. If stimulation was continued in monkeys, and always in cats, a true nystagmus with a swift component to the side opposite to the original deviation developed. With cessation of stimulation it was usually accompanied by post-nystagmus which lasted several seconds.

Small doses of nembutal markedly weakened the oculomotor effects of stimulation of ampullar nerves. A dose of 8 mg/kg brought /166
the extra-ocular potential to zero with a stimulation frequency by paired impulses of 40/sec, but a frequency of 77 pair/sec was still effective for the activation of extra-ocular potentials; nevertheless, the latency of the resulting muscular activity increased and the amplitude decreased. Group stimulations elicited only a slow deviation of the eyes. Nystagmus and post-nystagmus were not observed, and the eyes slowly returned to the middle position during stimulation. The nembutal effect had a central origin, insofar as the activity in the vestibular nerve was not changed even with deep anaesthesia: potentials of the 8th nerve registered after stimulation of the ampullar nerve of a cat with a frequency of 1 and 250 Hz did not change even with a dose of 30 mg/kg.

Thus, in a sleeping or anaesthetized animal a swift phase of nystagmus disappears, and the tonic motions corresponding to the slow phase of nystagmus can be investigated in relative isolation. By strictly dosing the electrical stimuli and measuring the corresponding directions of the muscles it is possible to indirectly analyze the nerve mechanisms of the vestibulo-ocular reflector arc. Moreover, insofar as eye motions elicited by stimulation of the ampullar nerve can be compared with compensatory motions of the

eyes arising with angular accelerations, then it is possible to define and measure the functionally important parameters of the response. Of these parameters the angular velocity of the eye, with the motion of the target relative to the retina, is considered to be the most important. Actually only in the case where the angular velocity of the eyes corresponds to the speed of the target is visual fixation of the moving object possible. The semicircular canals by themselves do not ensure the speed of the eyes necessary for the conclusion of ocular compensation during angular acceleration (Henriksson, 1955). This is possible only when the animal (man) sees the surroundings, i.e., when the opto-kinetic response is superimposed on the rotational response (Henriksson, 1955). The connection of the angular velocity of the eye elicited by rotation without visual stimulation with the angular velocity of rotation varies with different positions of the head and from animal to animal. Nonetheless, in a real animal with a fixed position of the head during rotation with a constant angular acceleration, the angular velocity of the eyes elicited by stimulation of the sensory structures of the semicircular canals in a sufficiently broad range of angular accelerations is strictly connected with the rotation velocity (Henriksson, 1955).

Thus, with investigation of eye responses of individual semicircular canals, the absolute value of angular velocity of the eyes during acceleration probably is less significant in comparison with the change of angular velocities of the eye with various amounts of stimulation. Guided by such considerations, Suzuki and Cohen /167 (1966) investigated contractions of the eye muscles which are primarily responsible for those of other eye motions elicited by stimulation of the ampullar nerves of the semicircular canal (Fig. 53). Insofar as the given muscles provide for motion of the eyes, the amount of their contraction must precisely reflect the amplitude of deviation and the speed of contraction, i.e., the angular velocity of the eye. Therefore, Suzuki and Cohen in their investigations were interested not in the absolute values of contractions and its speed, but in the changes elicited by stimulation of the nerve with various frequencies.

The authors showed that with electrical stimulation of the ampullar nerves in the absence of nystagmus, the speed of contraction of the eye muscles increases linearly for a certain period of time, attains a maximum and then decreases; i.e., it is possible to assume that impulses travelling along the ampullar nerves are integrated by the central vestibulo-oculomotor system, so that as a result of this integration there is motion of the eye with a definite speed proportional to the number of impulses arriving in the brain stem. Experimental results and empirical equations obtained by the authors for the size and speed of muscular contractions testify to the fact that the slope of the linear portion of curves of muscular contraction speeds depends upon the frequency of stimulation. Thus, the tempo with which central excitation increases appears as a function of the frequency, i.e., intensity of stimulation. However the tempo

of increased central excitation depended not only on the preceding stimulations, but also on the level of alertness, etc.

Between the value of maximum contraction speed and the frequency of stimulation there is also, as the authors indicated, a linear connection. During tonic deviations this was partically due to the inability of the eye muscles to continue contraction with increasing speed. However, the same connection between the maximum contraction speed and the frequency was observed even with electrically induced nystagmus (Cohen et al., 1965) so that even the level of central excitation was limited in the usual way. Even the presence of the linear connection between the logarithm of time from the beginning of stimulation to the moment of attaining maximum contraction speed of the muscle and the logarithm of the frequency of stimulation testifies to the limitation of integration. This dependency is close to a hyperberbola, i.e., the maximum contraction speed for each frequency of stimulation is attained by a relatively constant number of impulses (approximately 10,000 impulses in the experiments of Cohen and Suzuki).

It is interesting to consider the nature of neural activity which immediately produces muscular contraction. The authors did not obtain direct information on the type of nerve output to the muscles which produces either constant increase of strain or linearly growing speeds of contraction, but they did compare the curves of contraction obtained with stimulation of the ampullar nerves and stimulation of the motor nerves. /168

Such an analysis led the authors to the conclusion that with high frequencies of stimulation, each stimulus of the ocular nerves produces a corresponding impulse in the activating fibers of the ocular muscles. This indicates the high synaptic reliability of the multisynaptic vestibulo-ocular reflector arc, and moreover attests to the fact that the output of the oculomotor nerve, at least at the highest frequencies of stimulation, reaches a certain maximum frequency and then remains constant during the action of the stimulus.

The investigations of Suzuki and Cohen (1966) on electrically elicited eye motions demonstrated the close connections between frequency of stimulation and speed of contraction of ocular muscles, i.e., between the force of the stimulus and the output of the central formations responsible for tonic deviations of the eyes and the slow phase of nystagmus.

Investigations showed that the angular velocity of the eye is probably a more important parameter demonstrating the integratedness of the vestibulo-ocular reflector arc.

Certainly between the ampullar nerve activity, elicited by action of an adequate stimulus (constant angular acceleration) and electrical stimulation of the nerve there are a large number of differences. Thus under the action of constant angular acceleration,

the impulse frequency of the nerve slowly grows to maximum value (cf. Chapter II). With electrical stimulation impulses of the same frequency, equal to the frequency of stimulation go along all fibers of the nerve since angular acceleration elicits a spectrum of frequencies in the excited nerve fibers and not a unique frequency of activation (cf. Chapter II). Electrical stimulation adds impulses to the nerves of only one semicircular canal and does not decrease activity in the nerve of the contralateral canal lying in a parallel plane which would be produced during accelerated rotation. The efferent vestibular nerve activity also would not influence the impulsation frequency of the ampullar nerve with electrical stimulation.

Despite the differences existing between ampullar nerve activity elicited by electrical stimulation and angular acceleration, nystagmus induced by a gradual increase in frequency in the ampullar nerve of cats (Cohen, et al., 1965) and of rabbits (Levashov, 1965) has a surprising resemblance to nystagmus elicited by constant calaric stimulation or rotation at a constant angular velocity. Attacks of nystagmus have typically slow and fast phases, and even post-nystagmus is observed (Cohen, Suzuki, 1963; Cohen et al, 1965). The frequency of electrically produced nystagmus, as of nystagmus elicited by acceleration (Torok, 1948), at first is increased, obtaining a certain maximal value, and the amplitude and the speed of contraction of the muscles in the slow phase which reflect the amplitude and speed of the slow phase of nystagmus, at first increase linearly, then asymptotically approached maximum values with constant stimulation. As in natural nystagmus elicited by angular acceleration, the speed of the slow phase linearly increases in broader ranges with an increase in the frequency of stimulation than the amplitude of attacks (Henriksson, 1955). /169

The great difference between electrically elicited natural nystagmus, evidently, lies in the temporal passage of the excitation. The maximum speed of contraction with stimulation of the ampullar nerve was usually attained by the muscle under investigation after 3-5 seconds in the experiments of Suzuki and Cohen (1966), while with slow prolonged accelerations after 15-30 seconds, i.e., 5 times greater (Ek et al., 1960; Collins, Guedry, 1962). McCabe, (1965) on the basis of the analysis of the extensive literary data and the results of his own experiments on cats with electrolytic injuries of various vestibular muclei of the reticular formation of the brain stem, and also of investigations of the action of chemical preparations on the fast and slow components of nystagmus, came to the conclusion that the reticular formation is necessary for the appearance of a fast component.

As is well-known, there are two large paths along which the impulses from the vestibular nuclei proceed to the nuclei of the ocular muscles: the medial longitudinal bundle and the reticular formation (Carpenter, 1960). McCabe proposes that the reticular path conducts a certain portion of the impulses for a realization

of the slow components of nystagmus and all impulsation for the realization of the swift component; the medial longitudinal bundle conducts only impulses of the slow component. The conclusion of the author is corroborated by the experiments of Duensing and Schaefer (1957a, b), which described two types of neurons of the reticular formation: neurons firmly connected with nystagmus, which are activated during the swift phase and are inhibited during the slow phase of nystagmus, and neurons with the opposite characteristics. Moreover, there are neurons freely connected with nystagmus. Such neurons react both to acoustic and to auditory stimulation, and to the general condition of the animal, whereby the neurons which are activated during the time of arousal during the swift phase of nystagmus become still more activated, and those which are inhibited during the time of arousal become still more inhibited. McCabe proposes that the mechanism of nystagmus depends on the interaction between the neurons of the vestibular nuclei and the high threshold neurons of the reticular formation. Afferent impulses

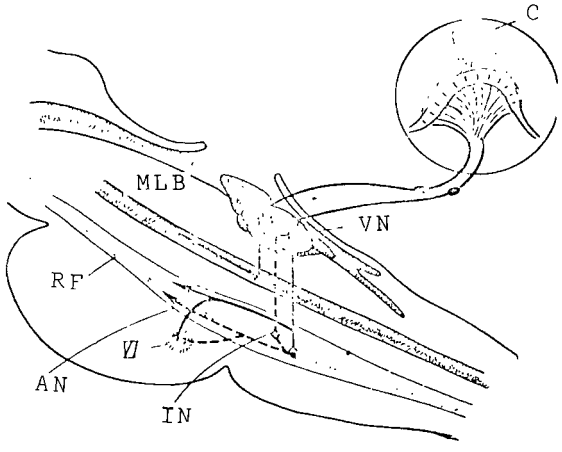

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Fig. 55. The Hypothesis of the Appearance of the Swift Phase of Nystagmus (McCabe, 1965). C - Cupula; MLB - Medial Longitudinal Bundle; RF - Reticular Formation; AN - Activating Neuron of the Reticular Formation; IN - Inhibiting Neuron of the Reticular Formation; VN - Vestibular Nuclei; VI - Nucleus of the Sixth Nerve; the Dotted Line Designates the Neurons Providing the Swift Components of Nystagmus; the Solid Lines, the Slow Components.

going to the nuclei of the ocular muscles through the medial longitudinal bundle lead to slow deflection of the eyes from the central position. High threshold reticular neurons, upon attaining the threshold, activate antagonistic muscles through contralateral oculomotor nuclei and simultaneously include inhibitory neurons of the reticular formation which interrupt the flow of impulses of the slow component (Fig. 55). The first nystagmic cycle is born. Reticular neuron which has discharged returns to its original condition; then

its threshold is reached again and the following cycle begins, etc. This character of dynamic rhythmic inhibition of the slow phase and the initiation of the swift phase with the aid of neurons of the reticular formation continues up to the time when the afferent input from the vestibular nuclei lowers to the rest level.

The author emphasizes that his own experiments do not give direct proof of the fact that the neurons of the reticular formation initiate the swift phase, but rather they indicate the importance of the reticular formation in the regulation of impulsation of the neurons of the vestibular nuclei. The worth of the hypothesis is in the fact that it connects many available anatomical and physiological data to this question. /171 In particular, several results of research in which attention was directed to the study of the role of the labyrinth receptors in the origin not only of the slow but also of the swift component of nystagmus began to be explainable (Koike, 1959; Levashov, 1964, 1965, 1967).

Mechanisms of Central Compensation of the Vestibular Function After Unilateral Labyrinthectomy

The study of compensatory reactions of an organism permits us to discover several characteristics in the activity of the nervous system which do not appear under ordinary conditions. It is known that the medulla oblongata plays an important role in the coordination of many vitally important functions of the organism, therefore investigations into the development of reflector mechanisms of compensation, in which primarily a given level of the nervous system takes part, present significant interest.

A group of vestibular nuclei located in the medulla oblongata serves as the place for completion of a number of labyrinth reflexes, one of which is the nystagmic motion of the eyes arising in response to stimulation of the semicircular canals of the labyrinth. Evaluating spontaneous nystagmus and also post-rotatory nystagmus in rabbits with rotation to both sides in various periods after unilateral labyrinthectomy, it is possible to judge the dynamics of compensatory processes the nervous system developed after the operation (Grigor'ev, Galiciy, Shipov, 1968).

Experiments were conducted on 59 male rabbits of the Chinchilla breed weighing up 3.2 kg. The experimental group of animals included 30 rabbits who underwent complete destruction of the left labyrinth; the control group included 20 intact rabbits. The operation was performed under sterile conditions using local anesthesia. Section was conducted through the left external acoustic meatus. The membranous labyrinth was brought under visual control through the oval window.

For confirmation of the authenticity of the operation, histological control was observed, showing complete destruction of all structures of the vestibular apparatus.

In two days, when the specific symptons of the rabbits elicited by the operational interference leveled off, they were investigated on a VU-2 rotating apparatus (Grigor'ev, Bokov, 1961). In order to do this they fixed the rabbit on a removable stand, located in a /172 room impenetrable to light and sound. The vertical axis of rotation passed through the center line uniting both labyrinths. The animals were rotated in a horizontal plane, alternately to both sides, beginning counterclockwise from an angular acceleration of 5 °/sec up to a given value of angular velocity. After equal rotation for 1 minute, the stand was brought to a sudden stop (stop stimulus) for 0.15 sec. The post-nystagmus arising from this was registered on the electroencephalograph made by "Kaiser's Laboratorium" with a time constant of 0.6. The root-orientational potential was removed with the aid of needle electrodes introduced into the skin of the forward and rear corners of the eye.

For the amount of stop stimulus they applied the value of angular velocity of equal rotation (van Egmond et al, 1949). The threshold of nystagmus was defined by the subsequent stimuli beginning at 5 °/sec. Then they studied the reactions of the animals to a number of stimuli increasing in value: 30, 60, 120, 180 °/sec. The time interval between stimuli was 1.5 - 2.0 min. Parameters of rotation were assigned with the aid of an electron-direction panel.

The animals were tested on the third, fifth, eighth and tenth day after the operation, and then each week up to the appearance of stabilization in reflector response of the vestibular analyzer with rotation to both sides. Moreover, from the time of the operation the recording of spontaneous nystagmus was performed daily.

Investigation of the rabbits in the control group was conducted according to the same system.

Nystagmic reactions were evaluated according to the threshold sensitivity, duration, and quantity of attacks. The obtained material was interpreted statistically by the student method.

Immediately after destruction of the left labyrinth in the rabbit, spontaneous nystagmus appeared directed to the intact side, which was easily discerned with the naked eye. In addition, the registered nystagmogram was presented as a sawtooth curve with sharply pronounced fast and slow phases.

In time the frequency and amplitude of spontaneous nystagmus decreased, and toward the end of the first week after the operation spontaneous nystagmus was not visually discovered in the majority of cases, although on the nystagmogram infrequent attacks were noted with the fast phase almost absent. During the eighth to tenth day, the curve of the recording of the rabbit's eye motion presented a straight line which indicated the absence of spontaneous nystagmus under our conditions (Fig. 56).

On the first day after the operation with rotation toward the side of the intact labyrinth, post-rotatory nystagmus did not arise, but the frequency of amplitude of spontaneous nystagmus decreased. With large stop stimuli (120 and 180 °/sec) even temporary disappearance of spontaneous nystagmus was observed (Fig. 57b). Rotation

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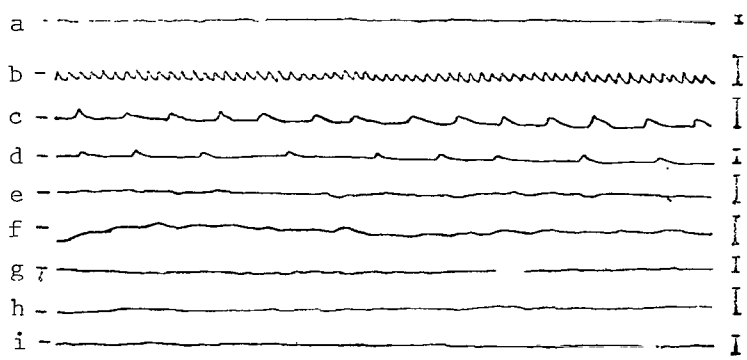

Fig. 56. Character of Spontaneous Nystagmus in Various Periods After Unilateral Labyrinthectomy. (a) Before the Operation; (b,c,d, e,f,g,h,i) Every Two Hours of Day #1, 2, 3, 4, 5, 6, 7, and 8 After the Operation. Calibration: 200 μV Scale of Time: 1 sec. (Grigor'ev Galichiy, Shipov, 1968).

towards the side of the destroyed labyrinth elicited post-nystagmus, corresponding in direction with spontaneous nystagmus. In addition frequency noticeably increased which appeared to be the criterion for a definition of post-rotatory nystagmus (Fig. 57b).

The duration of reaction was measured by the time interval during which the frequency of nystagmus in response to stop stimulus returned to the frequency of spontaneous nystagmus. For this interval of time the number of attacks was calculated. Definition of the duration of the post-rotatory nystagmus began 1 week after destruction of the labyrinth when the frequency of spontaneous nystagmus was substantially lower than the frequency of post-rotatory nystagmus. For the definition of the threshold of post-nystagmus, the stop stimulus was made immediately after registration of the next surge of spontaneous nystagmus. The supplementary attack following it directly was considered to be a post-rotatory reaction, and the value of stop stimulus to be threshold. Moreover the configuration of the nystagmic attack elicited by the stop stimulus often differed from that of spontaneous nystagmus.

Investigation on the 3rd day after the operation showed that with rotation to the left, the threshold value of stimulus was equal to 9.2 ± 0.9 °/sec, and with rotation to the right, 35 ± 7.3 °/sec. The difference between these reactions was statistically reliable ($p < 0.05$). The number of attacks of post-rotatory to the left and

right, respectively, was 10.0 ± 4.0 and 3.1 ± 1.5 ($p < 0.05$).

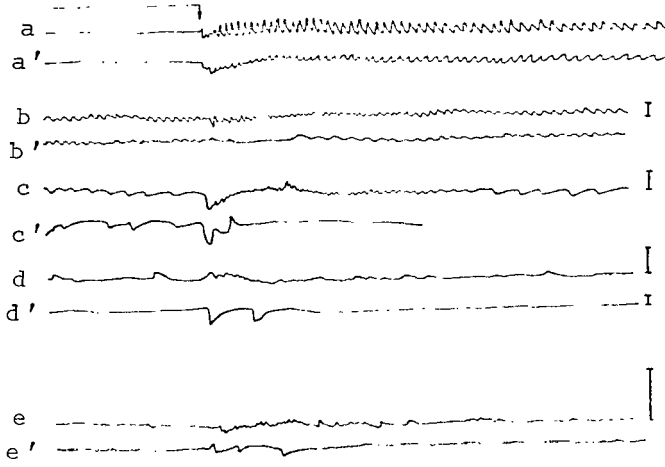

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Fig. 57. Post-Rotatory Nystagmus in Unilaterally Delabyrinthized Rabbits in Various Periods After the Operation. (a) Before the Operation; (b,c,d,e) Every Two Hours on Day #3,5,8 After the Operation; (a,b,c,d,e) Left Rotation; (a', b', c', d', e') Right Rotation. Calibration: 300 μV. Scale of Time 1 sec (Grigorius, Galechi, Shepov, 1968)

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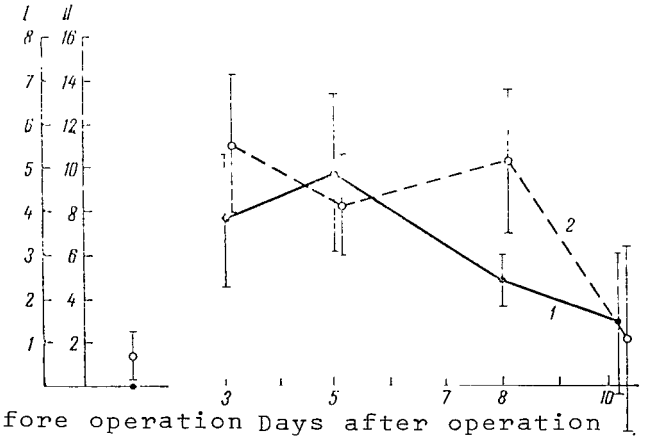

Fig. 58. Difference Between Nystagmic Reactions of Unilaterally Delabyrinthized Rabbits with Rotation to Both Sides in Different Periods After the Operation. Along the Ordinate Axis (I,1) - Difference of Threshold Values of Acceleration with Rotation Clockwise and Counter-Clockwise, Referred to the value of the Threshold Before the Operation; (II,2) - Difference Between the Number of Attacks of Post-Nystagmus Reaction with Rotation to Both Sides (Stop Stimulus 60 °/sec) (Grigor'ev, Galichiy, Shipov, 1968).

On the 5th and 8th day after the operation, the differences between nystagmus reactions of left and right rotation in threshold sensitivity values and the number of attacks per stop stimulus at 60 °/sec (Fig. 58) were statistically reliable ($p < 0.05$); stimulus at 120 °/sec were reliable only on the 8th day after the operation.

In further post-rotatory reaction, characterized by the number of nystagmus attacks, reliable differences were shown with stop stimulus of 60 °/sec during the fourth week of the investigation; with stop stimulus of 120 °/sec for the 4th, 6th, 15th and 20th week; and with stop-stimulus of 180 °/sec for the 6th, 13th and 17th weeks.

Differences in duration of the post-rotatory nystagmus with rotation to both sides for stop-stimulus of 60 °/sec were unreliable during the entire period of investigations beginning with the third week ($p < 0.05$), for stop stimulus 120 °/sec reliable for the 6th and 8th week, for stop stimulus 180 °/sec reliable for the 13th week ($p < 0.05$).

Four, five and six months after the unilateral labyrinthectomy operation, stable equilibrium was formed in the rabbits in reactions of post-nystagmus with rotation to both sides, both in threshold sensitivity and in duration and number of attacks. Moreover, post-

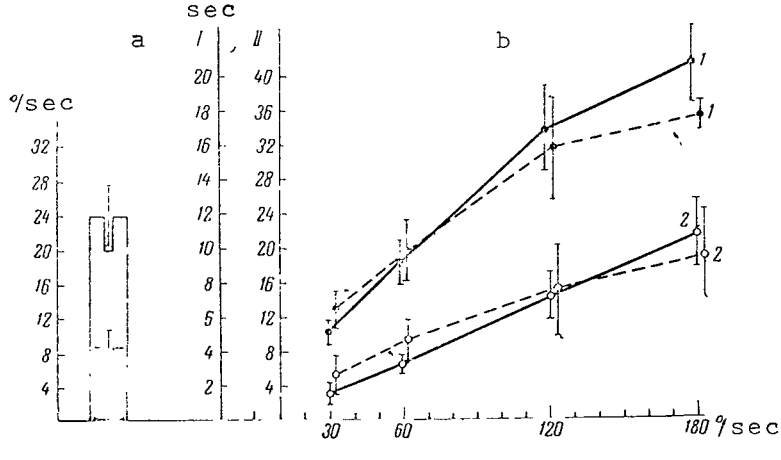

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Fig. 59. Comparative Characteristics of Post-Nystagmic Reactions in Intact and Unilaterally Delabyrinthized Rabbits After Compensation. (a) Threshold Reactions (the Black Column-the Rabbits Which Underwent Operation); (b) Duration (Scale I, the Dotted Curves) and Number of Strokes (Scale II, Solid Curves) Before (1) and 4, 5, 6 Months After the Operation (2) (Grigor'ev, Golichiy, Shipov, 1968).

rotatory reactions of unilaterally delabyrinthized rabbits decreased in comparison with reactions of intact rabbits by 2-3 times, (Fig. 59, a and b).

In animals of the control group, throughout the investigation no changes were observed in the equality of post-rotatory reactions of both sides.

As was shown in Chapter II, in the vestibular nerve at rest there exists an activity increasing with ampullopetal and decreasing with ampullofugal currents of the endolymph in the horizontal semicircular canal. In addition the dependency of the impulsation frequency in the nerve trunk on the value of stop stimulus is characterized the same as in a single fiber of the vestibular nerve, by an S-shaped curve (cf. Fib. 24, Chapter II). Since between the functioning of Type I neurons of the vestibular nuclei and in single nerve fibers there is a principal resemblance (cf. Chapter III), we considered it possible to present the combined activity of the neurons of the vestibular nuclei by means of S-shaped curves (Fig. 60).

In the rest condition the vestibular nuclei of both sides has equal activity (Ewald, 1892; Bechterev, 1909; Eckel, 1954). With destructin of the balance between these, two nystagmatic eye movements arise, the duration of which is defined by the time of the existence of difference in the activity of the nuclei (Lowenstein, 1937). The duration of post-rotatory nystagmus, thus, will be /177
defined by the time of the return of the cupula to a state of rest, and the dependency of the duration of nystagmus upon the amount of stop stimulus must be represented by a logarithmic function (Chapter II, Formula (9)).

After the destruction of one labyrinth, the amount of active neurons of the ipsilateral nucleus is substantially lowered in the time when the activity of the contralateral nucleus remains almost constant (Gernandt, Thulin, 1952; Shimazu, Precht, 1966; Precht et al., 1966). This destruction of balance between the vestibular nuclei leads to the appearance of a number of symptoms (deviation of the eyes, inclination and rotation of the head in relation to the trunk, differences in the tone of extremities, etc.,), including spontaneous nystagmus (Magnus, 1962).

Immediately after unilateral labyrinthectomy, spontaneous nystagmus arises which is directed towards the healthy (right) labyrinth. In addition, the difference of activities of the nuclei which arises is equal to 4 arbitrary units (Fig. 60). Insofar as it is assumed that during this time activity in the left nucleus is absent, the summary characteristic curve of the nuclei is defined by Curve I (Fig. 60). Then a stop stimulus of sufficient size (-5 arbitrary units) with rotation toward the side of the intact right labyrinth can only remove the activity of the right nucleus. In this case spontaneous nystagmus must disappear. Actually this fact is discovered with the investigation of rabbits on the first day after the operation (Fig. 57b), and this was also observed with rotation of pigeons (Schiebeek, 1953), of cats (Precht et al, 1966) and in pigeons with calarization of an intact ear by cold water (Fluur, 1960). However, eliciting post-rotatory nystagmus in a

direction opposite that of spontaneous nystagmus has not successfully been done at this time. After cessation of rotation, toward the side of the damaged labyrinth the difference of activities of the nuclei

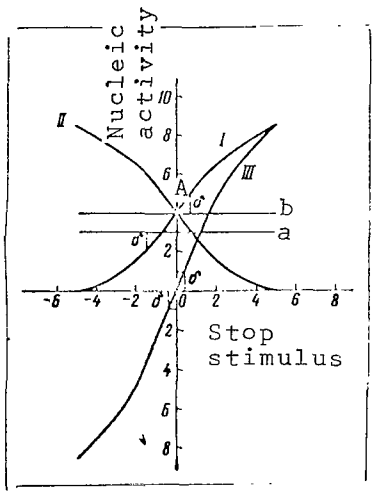

Fig. 60. Characteristic Curves of the Vestibular Nuclei. I - Right Nucleus; II - Left Nucleus; III - Summary Characteristic Curve, the Upper Branch of Which Indicates the Predominance of Activity in the Right Nucleus, the Lower and the Left; (a) Activity of the Left Nucleus in the Intermediate Stage and (b) on the Completion of Compensation (the Negative Value of Stop Stimulus Corresponds to Rotation to the Left) (Grigor'ev, Galichiy, Shipov, 1968).

increases (right branch of Curve I, /178
Fig. 60) which leads to an increase in the frequency of spontaneous nystagmus (Fig. 57b). Analogous observations were made by Precht and coll. (1966) on cats.

Toward the end of the first week the intensity of spontaneous nystagmus decreases so much that it can no longer be observed visually and can only be registered on a nystagmogram in the form of infrequent attacks. This is due to the restoration of activity of the vestibular nucleus of the destroyed left labyrinth (Spiegel, Demetriades, 1925), the reactivation of which is accomplished as a result of the action of the nucleus of the intact side upon it, of the reticular formation closely connected with both nuclei and also of other systems of the nervous systems (Fluur, 1960, Precht et al., 1966).

Evidently up to this time, in the nucleus on the side of the destroyed labyrinth, there is composite activity which, to a definite degree, must level the activity of the right nucleus (we supposed that it corresponds to the Level 2 in Fig. 60). Then if the value of this activity is equal to or greater than a certain value (δ) of the difference of activities of both nuclei, necessary for the appearance of nystagmus, then a stop stimulus to the right of sufficient size (-2 arbitrary units, Fig. 60) can elicit nystagmus to the side of the absent labyrinth. Indeed, on the 3rd, 5th, and 8th day after the operation it was possible to elicit post-nystagmus in the side of the destroyed labyrinth (Fig. 57 c,d). However it significantly differs in size from nystagmus in the opposite direction, which testifies to the absence of complete balance between the vestibular nuclei of both sides. This is also confirmed by the fact that on the 8th and 10th days after the operation, with an insignificant functional load (stop stimulus of small size), and

sometimes simply with the exclusion of light, spontaneous nystagmus appears which may be observed under the usual conditions (Fig. 61).

Two weeks after the operation, similar phenomena were noted in patients when they closed their eyes (Fluur, 1960).

In time the level of activity of the ipsilateral nucleus increases all the more corresponding to the level of activity of the contralateral nucleus (Level b, Fig. 60); in the activity of both nuclei equilibrium begins. Thus threshold reactions of nystagmus prove to be balanced during many weeks of the investigation beginning with the 10th post-operative day as well as post-rotatory nystagmus characterized by duration and quantity of attacks in response to stop stimulus of 60 °/sec. However, application of a

/179

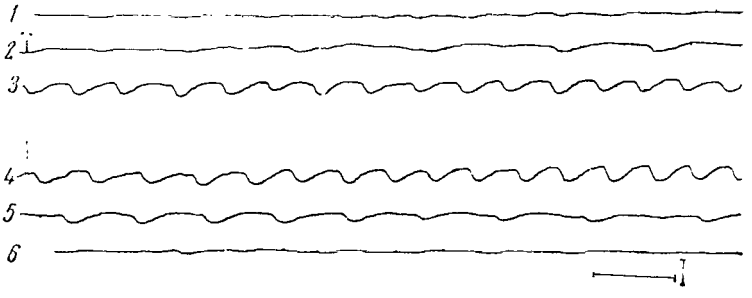

Fig. 61. Temporary Decompensation in a Unilaterally Delabyrinthized Rabbit (Galichiy, 1968). (1) Nystagmogram of a Rabbit on 3rd Day After Operation with Light Included; (2) Immediately After Exclusion of Light; (3) On the 56th Second After Exclusion; (4) Immediately After Inclusion of Light (Arrow Upwards); (5) On the 29th Second After Inclusion; (6) the 68th Second after Inclusion. Calibration 200 μV, Time Scale: 1 sec.

significant functional load (stop stimulus 120 and 180 °/sec) can elicit disturbances of balanced activity of the nuclei of both sides.

After 20 post-operative weeks, differences between nystagmic reactions of the left and right rotations could not be registered with an applied stimuli. Consequently 4,5, or 6 months after unilateral destruction of the labyrinth in rabbits, stable equilibrium is formed between nystagmic reactions with rotation to both sides. The stability of the mechanisms formed for compensation is so significant that general gamma radiation with an 800 R dose (power of the dose: 180 - 200 R/min) does not change the established equilibrium of nystagmatic reactions (Galichiy, Shipov, Tabakova, 1966; Galichiy, 1966a). Only the action of a dose of 1600 R (Galichiy 1966b) in some unilaterally delabyrinthized rabbits elicited the appearance of spontaneous nystagmus (Fig. 62), and in the majority of animals distinct destruction of equilibrium in post-nystagmus reaction (Fig. 63), whereby the character of the destruction of balance is similar to that observed immediately after unilateral

destruction of the labyrinth.

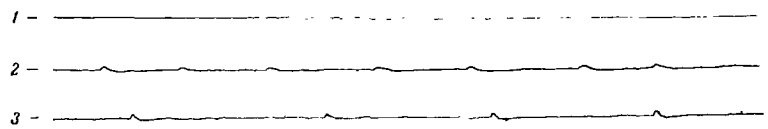

Fig. 62. Decompensation in a Unilaterally Delabyrinthized Rabbit After Radiation with a Dose of 1600 R (Galechi, 1968). (1) Nystagmogram of the Rabbit on the Third Day After the Operation (Before Radiation); (2) Every 4-5 Hours After Radiation; (3) On the 3rd Day After Radiation.

/180

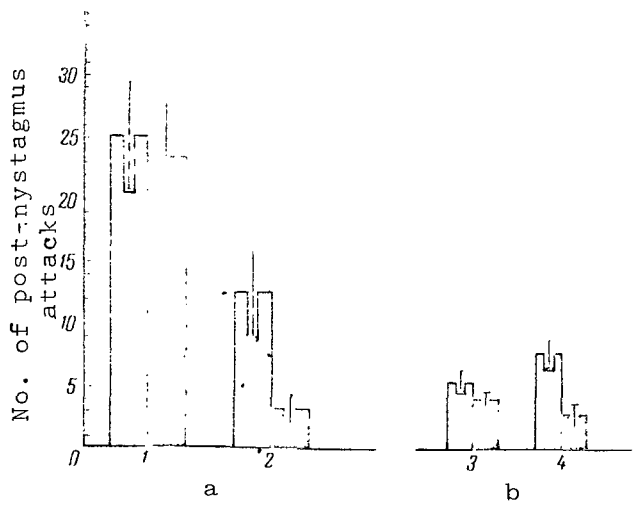

Fig. 63. Destruction of Equilibrium of Post-Nystagmatic Reactions in Unilaterally Delabyrinthized Rabbits, Irradiated 6 Months after the Operation. (1) Number of Post Nystagmus Attacks (Stop Stimulus 60 °/sec) in Intact Rabbits; (2) On the 3rd Day After Operation; (3) 6 Months After the Operation; (4) Every 4-5 Hours After Irradiation with a Dose of 1600 R. The Black Column: Left Rotation; the White: Right Rotation. (Galichiy, 1968).

The threshold sensitivity of unilaterally delabyrinthized rabbits lowers 2 1/2 times in comparison with the original level; the duration of nystagmus by 2.0 - 2.5 times, the amount of attacks by 2.0 - 3.0 times (Fig. 59).

The mathematical analysis of the dependency of the duration and number of post-nystagmus attacks upon the amount of stop stimulus for intact rabbits, conducted by B.B. Bokov and A.A. Shepov (1965), indicated that not one of the dependencies in the band of stimuli from 10 - 180 °/sec appears as a linear or logarithmic function. However a portion of the curves of the continuation of nystagmus in

a subrange of stimuli from 10 - 60 °/sec is best approximated by logarithmic functions. The curve of the number of nystagmus attacks in the same subrange can be approximated both by linear and by logarithmic functions. In the subrange of stimuli from 70-180 °/sec a linear approximation of both curves is possible. Precht and coll. (1966) showed that in unilaterally labyrinthized cats, the curve of prolongation of nystagmus in the compensation stage is also approximated by a logarithmic function (in the range from 50-200 °/sec).

If we assume that the threshold value of the difference between activities of vestibular nuclei (δ) in unilaterally delabyrinthized rabbits remains constant after completion of the compensatory process (Level b, Fig. 60), then the amount of stop stimulus eliciting the first nystagmic motion of the eyes will correspond to point A on Curve 1 (0.8 arbitrary units). This value is 2 times greater than the threshold stimulus defined according to Curve 3 in intact animals, i.e., it approximately equals with the results of the experiments. /181

It is possible to assume that a change in threshold sensitivity, duration and number of nystagmus attacks in response to stop stimulus in unilaterally delabyrinthized rabbits takes place mainly as a consequence of a two-fold decrease in the difference of the activities of the nuclei. This is confirmed by the investigations with unilateral binding of the horizontal semicircular canal,[7] which demonstrated the decrease and duration of post-rotatory nystagmus after the operation by 2 times (Money, Scott, 1962).

Figure 60 permits us to evaluate qualitatively the activity of the vestibular analyzer under normal conditions and during different periods after unilateral labyrinthectomy.

Characterizing post-nystagmus according to its duration, the destruction of equilibrium could be observed on the 6th, 8th and 13th week after the operation only with stimuli of great size. Using the number of post nystagmus attacks as a test, differences in the reactions of left and right rotations could be shown with the smallest functional load, even during the 20th week after the operation. Probably this indicates the fact that the method of evaluation of post-rotatory nystagmus according to the number of attacks characterizes the dynamics of the onset of compensatory mechanisms of the nervous system of unilaterally delabyrinthized rabbits more precisely than evaluation according to duration, and also that the mechanisms responsible for duration and frequency of nystagmus are relatively independent.

Using characteristics of post-nystagmus such as threshold

[7] A similar method of exclusion of one horizontal semicircular canal gives the possibility of leaving spontaneous activity of the nuclei of both sides unchanged.

sensitivity and number of attacks, it is possible to evaluate the condition of the mechanisms of compensation of the nervous system of the first days and weeks after unilateral destruction of a labyrinth. In the later periods it is necessary to apply a functional load, since under the usual conditions the degree of stability of the equilibrium produced cannot be analyzed. Thus, in order to more fully evaluate the functional condition of the vestibular analyzer /182 in unilaterally delabyrinthized animals, it is necessary to consider the combination of characteristic of post-rotatory nystagmus.

The participation of the higher sections of the central nervous system in the formation of compensatory processes with labyrinthal destructions was demonstrated in the whole series of investigations (Asratyan, 1947, 1960; Ayrapet'yants and Kislyakov, 1957; Kislyakov 1959 et al.). However, evaluating the role of definite levels of the nervous system in the formation of compensatory adaptations, it is important to consider the place occupied by the investigated objects in a phylogenetic series.

The more highly developed the central system, the greater is the participation of higher sections in adaptive reactions (Asratyan 1958). Experiments on rabbits and cats, using the method of excluding various sections of the nervous system (total removal of the cerebellum, vestibular nuclei of each side, pro and diencephalon, sections above the roof of the lamina quadrigemina) succeeded in showing that compensation of destroyed functions after unilateral labyrinthectomy appears only in the case when ipsilateral vestibular nuclei remain intact (Spiegel, Demetriades, 1925; Spiegel, Sato, 1927). Under these conditions, compensation began each time that the central nervous system of the overlying sections was not destroyed. This fact does not exclude participation in the development of compensatory adaptations of the higher sections of the nervous system. On the contrary, it is assumed that the restoration of activity of the nuclei on the side of the operation takes place as a result of influences from the cortex of the cerebral hemispheres, of subcortical nuclei, and the roof of the lamina quadrigemina, of the cerebellum, and of the contralateral vestibular nuclei (Spiegel, Demetriades, 1925), and also of the reticular formation of the brain stem (Fluur, 1961). Consequently the complex of vestibular nuclei introduced a very significant component into compensation for labyrinth destruction in animals of the given type.

The results of our investigations showed that in unilateral delabyrinthized rabbits after 4, 5 or 6 months, a balance in the activity of the vestibular analyzer begins. This allows us to assume that the medulla oblongata of rabbits possess as great compensatory capabilities. In addition, the stability of the mechanisms of compensation which were formed is so significant that none of the applied stimuli could again elicit functional destruction in the activity of the vestibular nuclei which existed immediately after the operation.

In the preceding chapter, several synaptic connections of the central vestibular neurons with the ipsilateral and contralateral horizontal semicircular canals which have been established to date were discussed. It was assumed that the vestibular Type II neurons /183 are inhibitory neurons conducting influences from the contralateral horizontal canal and acting on the chief sensory neuron (Type I) in the homolateral vestibular nuclei (Shimazu, Precht, 1966).

What functional changes take place in Type I and II neurons in the compensation stage after unilateral labyrinthectomy?

With the aim of clarifying this question, Precht, Shimazu and Markham (1966) experimented on labyrinthectomized cats with stimulation of the remaining labyrinth.

In 3-4 days and after 30-45 days after labyrinthectomy, motions of the eye were registered at rest, during acceleration, constant rotation velocity, and after a sudden stop. Special attention was given to the duration of the post-rotatory nystagmus with rotation to both sides.

After the vestibulo-ocular function was sufficiently compensated (usually after 30-45 days, which was judged by the equality of duration of nystagmus with rotation to both sides), fine experiments on decerebrated, decerebellized and nonanaesthesized preparations were completed.

The potentials elicited by electrical stimulation of the intact vestibular nerve in the ipsilateral and contralateral nerve were similar with those described in detail in Chapter III. Despite the careful study, the authors did not discover an essential difference in configuration, latent period, amplitude, or localization of elicited summary potentials in chronically, unilaterally delabyrinthized animals and animals with both labyrinths intact.

In acute experiments it was difficult to discover Type I neurons in the vestibular nuclei on the side of the destroyed labyrinth (Gernandt, Thulin, 1952; Shimazu, Precht, 1966). But 35-40 days after the operation, Type I neurons were easily registered both on the side of labyrinth injury as well as on the intact side (Precht, Shimazu, Markham, 1966). Responses of Type I neurons to rotational stimulation in animals with a chronically destroyed labyrinth, on the side of the injury, had characteristics similar to those obtained from animals with both labyrinths intact (Shimazu, Precht, 1966). However the maximum discharge frequencies of Type I neurons on the deafferentized side during ipsilateral horizontal angular rotation were around 25 Hz, i.e., much less than the discharge frequency (80 Hz or more) registered in animals with intact labyrinths. Insofar as with the given experimental conditions there are no influences of the ipsilateral labyrinth observed, changes in discharge frequency must be due to an increase or decrease of inhibitory influences from the contralateral horizontal canal during rotation (Shimazu, Precht, 1966).

The thresholds of frequency responses to horizontal angular accelerations of Type I neurons registering on the chronically delabyrinthized side usually fluctuated from 2 to 8 °/sec^2 and with an insignificant number of units, i.e., to 8 °/sec^2 and more. These values are essentially higher than the thresholds of tonic neurons in animals with intact labyrinths, (0.23 - 1 °/sec^2) and are very close to the thresholds of Type II neurons (cf. Chapter III). /184

The frequency of spontaneous discharge of Type I neurons on the delabyrinthized side was usually less than 10 Hz. High discharge frequencies (30 Hz and more), registered on the intact side, usually were not observed on the side of the injury under rest conditions.

Many Type I neurons on the side which was operated upon did not have spontaneous discharges, and their thresholds of frequency response were higher than the thresholds of tonic neurons in intact vestibular nuclei, which are similar to the characteristics of kinetic neurons. However the swift change in impulsation frequency characteristic of kinetic neurons with the action of acceleration and abrupt increase in maximal value of frequency with increase in the amount of acceleration was not observed. All this attests to the fact that Type I neurons without spontaneous discharges, discovered on the delabyrinthized side, were tonic in nature, but lost their activity due to the removal of the exciting influences from the ipsilateral labyrinth receptors. The authors could not identify kinetic neurons, probably due to the fact that their high thresholds to angular acceleration were still more elevated with destruction of the ipsilateral labyrinth.

Spontaneous activity of all Type I neurons registered on the side of the injury were clearly suppressed by electrical stimulation of the intact contralateral vestibular nerve.

It is improbable that the observed effect is due to presynaptic inhibition by means of depolarization of primary vestibular afferents, insofar as the histological control indicated complete degeneration of the vestibular nerve on the side of registration. Threshold stimuli of the vestibular nerve eliciting contralateral inhibition were 1 - 1.6 times higher than the threshold of the potential M_1 (on the average 1.35 ± 0.26). These values are significantly ($p < 0.001$) lower than those obtained from vestibular neurons in animals with both intact labyrinths: the range is 1.25 - 2.8 (on an average 1.99 ± 0.53).

After section of the brain stem along the central line from the inferior corpus bigeminum to the obex at a depth of 2 mm in chronically deafferentized vestibular nuclei, where before conducting the central sectioning many Type I units were discovered, identified by horizontal rotation, high frequency spontaneous discharges (20 Hz and greater) were often registered. These units discharging

with high frequency could not be identified any more due to their response to rotation, insofar as the vestibular nuclei were lacking both ipsilateral and contralateral influences. However judging by the location of these units in the vestibular nuclei, it is completely probable that at least several of them were Type I neurons and that the increase of frequency of spontaneous discharges after medial section was elicited by the removal of tonic inhibitory influences from the intact labyrinth through the commissural system (Shimazu and Precht, 1966). As was described above, the maximum discharge frequency of Type I units on the deafferentized side during ipsilateral angular rotation was around 25 Hz, i.e., of almost the same value as the maximum frequency of spontaneous activity after section of the commissural fibers. These data lead to the thought that a maximum increase in discharge frequency of Type I neurons during ipsilateral acceleration was produced by the lowering of inhibition to a minimum from the contralateral horizontal canal, thus eliciting the same effect as section of the commissural fibers. /185

Insofar as one labyrinth was destroyed, then rotational Type II responses on the side of the injury must be due to the exciting influences from the horizontal canal of the intact side. The thresholds of frequency responses to horizontal angular accelerations of Type II neurons registered on the chronically delabyrinthized side fluctuated from 1.7 to 10 $^{\circ}/sec^2$ or more. These values were almost identical to those obtained on animals with both labyrinths intact (Shimazu, Precht, 1966). The frequencies of spontaneous discharges of Type II neurons (0 to 30 Hz) also were similar to those of animals with intact labyrinths.

All Type II neurons registered on the side of injury were excited by electrical stimulation of the contralateral vestibular nerve. The thresholds for excitations of Type II neurons obtained with rhythmic stimulation at a frequency of 50 Hz were greater than the threshold M_1 by 1.57 ± 0.41 times. Statistically these values did not differ ($p < 0.7$) from the threshold (1.52 ± 0.17) of Type II neurons in animals with intact labyrinths, which were connected exclusively with the commissural system.

Thus, fine distinctions and the activity of the vestibular nerves in chronically unilaterally delabyrinthized animals and animals with both labyrinths intact or with acute unilateral delabyrinthization can be defined by the following two criteria: (1) spontaneous discharges of Type I neurons and their partial responses to horizontal angular acceleration were more easily discovered in chronically deafferentized vestibular nuclei than in sharply deafferentized nuclei; (2) thresholds for inhibition of Type I neurons with electrical stimulation fo the intact contralateral vestibular nerve in chronically deafferentized vestibular nuclei were significantly lower than those observed in animals with intact bilateral labyrinths.

It is well known that functional changes in the central neurons due to long-term injury of the conducting structures are due to /186
degeneration of the synaptic endings on the neurons. Degeneration of some of the afferent fibers leads to an increase in the sensitivity of the post-synaptic membrane to chemical actions (Kennon, Rozenduk, 1951; Drake, Stavraki, 1948), and also to germination of the collateral of the neighboring desynaptic fibers (Liu, Chambers, 1955; McCouch et al., 1958). In the investigations under consideration, degeneration of afferent fibers from the destroyed labyrinth inside the brain stem were histologically indicated. The restoration of spontaneous discharges of Type I neurons after degeneration of the chief exciting sensory input can be elicited by biochemical sensibilization of deafferentized Type I neurons or by the generation of other afferent fibers, for example, reticular vestibular ones. Reticular vestibular connections not only are anatomically established (Lorente de No. 1933 b) but also, found physiologically, are exciting (Markham, Precht, Shimazu, 1966; Shimazu, Precht, 1966). Dolman (1929) found that even after bilateral labyrinthectomy, intercranial section of the 8th nerve on one side leads to the same motor destruction as with unilateral labyrinthectomy. Therefore he assumed that after removal of the labyrinth, the tonic activity of the cells of g. Scarpa does not disappear. It might be possible that the disappearance of spontaneous nystagmus only after 2-3 days after unilateral labyrinthectomy was partially due to elevated activity of discharges of the cell of g. Scarpa on the side of the injury. However spontaneous activity, observed 30-45 days after an operation must be explained by internal mechanisms on the level of the vestibular nuclei, insofar as the effect of intercranial neurotomy, discovered by Dolman several days after the original labyrinthectomy, is gradually weakened and becomes scarcely noticeable at a later stage of compensation. Clear degeneration of the vestibular nerve in the brain stem also decreases the probability that spontaneous impulses of the vestibular nerve of the delabyrinthized side could be responsible for the restoration of activity of Type I neurons in the compensation stage.

Impulses from the horizontal canal activate the ipsilateral Type I neurons; the latter in turn send exciting impulses to the contralateral Type I neurons through the commissural fibers; and finally Type II neurons can inhibit Type I neurons on the same side (Shimazu, Precht, 1966). Any portion of this path may be res- /187
ponsible for lowering the thresholds of contralateral inhibition of Type I neurons. However, in the investigations of Precht, Shimazu and Markham (1966), contralaterally elicited initial positive summary potentials and subsequent negative waves in the ventral portion of the vestibular nuclei of the injured side did not differ in any way significantly from those obtained on animals with intact bilateral labyrinths. As was shown in the preceding section, the initial positive potential reflects the sum of action potentials of commissural fibers in the region of their endings, and the subsequent slow negative component reflects excitation of Type II neurons. Furthermore, thresholds of contralateral activation of Type

II neurons and chronically deafferentized vestibular nuclei are almost the same as those obtained in cats with intact labyrinths. These data show that significant functional injury did not take place either in the commissural fibers on the intact side nor in Type II neurons on the chronically deafferentized side. Consequently noticeable functional changes probably take place chiefly in Type I neurons on labyrinthectomized sides. This conclusion agrees with the assumption that long-term changes are produced in neurons which have synaptic contact by degenerated afferent fibers, insofar as Type II neurons which obtain the strongest exciting influences through the commissural fibers are connected exclusively with the contralateral labyrinth, and do not have direct connections with the ipsilateral vestibular nerve (Shimazu, Precht, 1966). However, in an insignificant number of Type II neurons a certain decrease in the duration of the latent period was noticed. It is possible that this is connected with an increase in the excitability of several Type II neurons which obtain afferent waves both from the commissural system and from the ipsilateral labyrinth.

One of the possible explanations of the lowered thresholds of contralateral inhibitions in Type I neurons is that degeneration of primary afferents stimulates degeneration of neighboring presynaptic fibers from Type II neurons, thus increasing inhibitory synaptic action in Type I neurons. /188 It follows also to consider the hypersensitivity of deafferentized Type I neurons both to exciting and to inhibiting synaptic actions. Furthermore, it is impossible to exclude the possibility that elevated excitability of several Type II neurons is partially connected with the increase of inhibiting action on Type I neurons. Although experiments of Precht, Shimazu and Markham (1966) do not supply an answer to the question of which of the enumerated mechanisms are realized in the activity, it is necessary to bear in mind that a long-term increase of inhibitory action may proceed from the central nervous system. The fact of an increase of exciting activity of the central nervous system is well-established at the present time.

In the compensation stage of vestibulo-ocular function, spontaneous discharges of Type I neurons in rest conditions on the side of the injury were still lower than on the intact side, partially due to highly developed inhibitory influences from the intact labyrinth. This phenomenon may be responsible for the incomplete restoration of postural symmetry. Nonetheless, the restoration of spontaneous discharges of Type I neurons evidently plays an important role in the central compensation for balanced activities of symmetrical vestibular nerves. These results confirm the assumption of Spiegel and Demetriades (1925). Moreover, it is justified to expect that in the compensation stage after labyrinthectomy a second operation of labyrinth destruction on the opposite side not only weakens spontaneous activity of Type I neurons on the side of the second operation, but also decreases contralateral inhibitory influence and facilitates the activity of Type I neurons on the side of the first operation, thus leading to Bechterev's compensatory nystagmus.

A similar explanation would be applied even to the data of Spiegel and Sata,(1927), but even after a sharp bilateral labyrinthectomy supplementary unilateral destruction of the vestibular nerves elicits nystagmus and deviation of the eyes. The concept of the liberation of Type I neurons from contralateral inhibition is strengthened by the fact that after section of the commissural fibers conducting these inhibitory influences, a noticeable increase in spontaneous activity of deafferentized vestibular neurons was discovered, and at least several of them were probably Type I neurons (Precht, Shimazu, Markham, 1966).

This assumption, finally, does not exclude the possibility that the cerebellum or other structures play an important role in the establishment of central compensation of vestibular function (Carpenter et al., 1959).

As far as accomplishment of restoration of symmetry in eye movements caused by stimulation of terminal organs of the semicircular canals is concerned, evidently it is essentially the fact that the remaining intact labyrinth controls not only the ipsilateral vestibular Type I neurons but also the contralateral Type I neurons reciprocally by means of the commissural inhibitory mechanism. Insofar as this inhibitory influence is developed very strongly in the compensation stage it may be sufficient to insure fully symmetrical control of the eye motions elicited by rotation.

Despite the fact that in recent years the most abundant material has been obtained on the investigation of the specific links of the vestibular oculomotor arc, any questions on the mechanisms /189
of eye motions elicited by stimulation of the vestibular apparatus are far from resolved. In particular, as before, the mechanism of the appearance of nystagmus is not clear.

Furthermore, progress in the understanding of this question is unconditionally connected with the investigation of the oculomotor apparatus as a whole. In this regard, the greatest help can be mathematical simulation of the oculomotor apparatus with the consequent testing of models upon computers. This path opens broad possibilities for experiments on machines and, on the other hand, gives physiology a means to create and test working hypotheses which will aid a directed experiment on animals.

CHAPTER V

CONNECTIONS OF THE LABYRINTH WITH THE SPINAL CORD

Morphology

Vestibulo-Spinal Projections. At the present time it is a generally acknowledged fact that the fibers going from the vestibular nuclei to the spinal cord may be divided into two systems: the vestibulo-spinal tract, and fibers descending in the medial longitudinal bundle and its continuation in the spinal cord. /190

The vestibulo-spinal tract proceeds ipsilaterally to the lower levels of the spinal cord in the ventral-lateral funiculus on the same side. The fibers of the vestibulo-spinal tract take the same position, passing in a ventral-medial direction from the point of their origin. Turning gradually in a caudal direction, they appear more dorsal-medial than the nucleus of the facial nerve. Continuing further in a caudal direction, the fibers are lowered in a more dorsal-medial direction than the nuc. ambigius, more lateral than the roots of the sublingual nerve fibers and more dorsal than the inferior olive. Furthermore, they pass more dorsal than the reticular lateral nucleus to which they yield collaterals. After entering the spinal cord, the majority of them may be discovered in the ventral half of the lateral funiculus, while other fibers descend in a medial direction from the place where the ventral roots appear. The vestibulo-spinal fibers were traced to the lower lumbar and sacral regions in animals and man (Brodal et al., 1966). It is necessary to note that the vestibulo-spinal tract in the lower regions of the spinal cord is displaced in a dorsal-medial direction. Ignorance of this fact often leads to unfortunate confusion (Nyberg-Hansen, 1964).

The majority of authors consider that the lateral nucleus is the source of the vestibulo-spinal tract.

It is known that the anterior portion of the cerebellum has somatotropic organization, and localized stimulation or separation of it is expressed by a change in muscle tone and myotactical reflexes of the anterior and posterior extremities. They assume that these influences were intermediated through the reticular formation. However, stimulation of the reticular formation did not show somatotropic localization in it (Sprague, Chambers, 1954); Brodal and

Torvik (1957) morphologically confirmed the absence of such localization. The fastigio-reticular system is also organized diffusely. The following question arose: cannot the vestibular nuclei which receive fibers from the cerebellum serve as an intermediary link for the transmission of somatically localized impulses from the forward portion of the cerebellum to the spinal cord? Such a conception assumes the presence of somatotropic localization from the lateral vestibular nucleus to the spinal cord. Somatotropic organization of the lateral nucleus was demonstrated (Brodal, 1964; Brodal et al, 1966) morphologically by applying a modified Gudden method. After sectioning the spinal cord of kittens they observed retrograde degeneration in Deiter's lateral nucleus. It was found that not only do gigantic cells of Deiter's nucleus send their axons into the spinal cord, but also the small ones. The projection of the nucleus to the spinal cord had a clear somatic localization: the rostral-ventral portion of the nucleus sent its fibers to the neck section of the spinal cord, the dorsal-caudal to the lumbosacral, the central portion to the thoracic. Thus the vestibulo-spinal projection corresponds to the demands of a somatotropic connection between the cerebellum and the spinal cord. Such a fact must be noted. The primary afferent fibers do not feed the zone of the "posterior extremity" in Deiter's nucleus, but are organized by the zone of the "anterior extremity", i.e. its rostral-ventral portion. According to the data of Lorente de No (1933a), the macula utriculus, which is important for tonic labyrinth reflexes, is the chief source of afferents to Deiter's nucleus. /191

Insofar as vestibular impulses influence not only the tonic and reflex activity of the cervical sections of the spinal cord, but also the lumbosacral sections, the following question arises: why do the primary vestibular fibers reach only the zones of the anterior extremity of Deiter's nucleus? Certainly this does not exclude vestibular influences on the cells of the dorsal-caudal portion of the nucleus, acting on the lumbosacral section. Dendrites of the cells in this zone may spread into the zone of the anterior extremity and into other regions of the vestibular complex receiving primary fibers. Cajal (1909) mentioned that dendrites of the cells of the lateral nucleus in the mouse may spread beyond its territory and enter medial and descending nuclei. However, Brodal et al. (1966) did not corroborate this for cats: all cells of Deiter's nucleus limited the dendrites to Deiter's nucleus alone.

The lateral vestibular nucleus influences myotactic reflexes and muscle tone activating both alpha and gamma neurons of the spinal cord (Andersson, Gernandt, 1956). Therefore it was of interest, considering the influences of the lateral vestibular nucleus on the spinal cord, to explain where and how the vestibulo-spinal fibers terminate in the spinal cord. Nyberg-Hansen and Mascitti (1964), /192 in Brodal's laboratory, used the Naut-Gliss method to study the locations of the vestibulo-spinal fiber endings after electrolytic destruction of the vestibular nucleus, according to systems of

cytoarchitectonic laminae of the gray matter of spinal cord segments proposed by Rexed (1954).[8] After destruction of Deiter's nucleus, degeneration of fibers was discovered exclusively in the ipsilateral vestibulo-spinal bundle. Degeneration of preterminal and terminal fibers was observed only in Laminae VII and VIII. Neurons of these laminae are intercalory. Degenerative changes neither in the gamma motoneurons nor in the medial neurons were discovered. In the cervical and lumbar sections, degeneration was more pronounced than in the thoracic section. The basic type of degenerated synapsis was exodendrite, but axosymmatic were also found.

Fibers of the descending medial longitudinal bundle are directed medially or somewhat ventral-medially and are gathered immediately lateral of the central line, ventral-medial in relation to the knee of the facial nerve. From this point the fibers descending to the spinal cord continue in the caudal direction near the central line. Then at the level of the pyramid intersection they are deflected in a lateral direction, from which they continue in the ventral funiculus of the spinal cord (this portion of the bundle is sometimes called the sulco-marginal bundle).

Nyberg-Hansen (1964), after electrolytic destruction of the four basic vestibular nuclei, traced the degeneration in the medial longitudinal bundle and its terminal and preterminal fibers in the segments of the spinal cord according to the Naut-Gliss method. The author confirmed the data of Carpenter and coll. (1960) that only the medial nucleus provided fibers descending in the medial longitudinal bundle both in the ipsi- and contralateral direction. In the lumbar section degeneration was not observed. Degenerated fibers went from the medial longitudinal bundle and entered the ventral column from the dorsal-medial side, corresponding to the dorsal half of Lamina VIII on both sides and also to Lamina VII. Degeneration was not traced either in the cells of the intermedial column or in Clark's column. The degenerated fibers terminated both in large and also in small cells. From a functional point of /193
view it is interesting to compare both systems which have vestibular influences on the spinal cord. The massive somatotopically organized vestibulo-spinal tract proceeds to the lower segments and departs from the lateral nucleus to which, basically, impulses from the macula utriculus proceed. The medial nucleus is subject to influences from the cristae of the semicircular canals and has a limited spinal projection not lower than the thoracic segments. However both descending tracts terminate on the 7th and 8th laminae and do not contact the motor neurons. From the available somatropic

[8] Laminae according to Rexed: (I) the summit of the dorsal column; (II) cells of the dorsal column corresponding to Rowland's substance; (III-IV) the basic mass of cells of the dorsal column; (V-VI) the foundation of the dorsal column; (VII) cells of the zona intermedia; (VIII) medial portions of the ventral column; (IX) the medial and lateral nuclei of the motor cells. Sizes of laminae on various levels of the spinal cord vary.

data, it is permissable to assume that along the paths of the fibers originating from the medial nucleus, impulses from the cristae of the semicircular canal influence the muscles of the neck and the forward extremities.

Spino-Vestibular Connections. The spino-vestibular fibers ascend with the fibers of the dorsal spinal cerebellar tract. The fibers to the vestibular nuclei may be represented by the collaterals of the dorsal spinal cerebellar fibers, but there is a certain number of direct spino-vestibular fibers. According to the data of Pompeiano and Brodal (1957) and Brodal and coll. (1966), a significant number of spino-vestibular fibers depart from the lumbosacral segments. It was discovered that the locations of the spino-vestibular fiber endings are territorially limited. The number of degenerating terminal fibers in the medial and descending nuclei is small, and their distribution is limited by the most caudal regions of these nuclei. In the lateral nucleus degeneration is also weak and is traced only in its dorsal and caudal-dorsal portions, i.e., in those regions which are not fed by the primary vestibular fibers. In the lateral vestibular nucleus the terminal degenerating fibers end in expanded compact terminal patches on the perikaryon of gigantic cells, and although such contacts are not observed on the smaller cells of a given nucleus the possibility is not excluded that spinal afferents accomplish synaptic contacts with such cells. Thus the terminal region of spinal afferents corresponds with that portion of the lateral nucleus which sends fibers to the lower levels of the spinal cord, i.e., with the region of the lower extremity of the nucleus. Insofar as the spinal vestibular fibers leave from the lower segments of the spinal cord, such observations allow us to suppose that the dorsal-caudal portion of the nucleus is functionally closely connected with the lower portion of the spinal cord and correspondingly with the lower extremity. The morphological data of Brodal and coll. (1966) are confirmed physiologically (Wilson, et al, 1966). It is possible that these spinal impulses are especially important for reflexes of the rear extremities realized through this nucleus, while for reflexes of the forward extremities, the vestibular impulses play a more important role.

In Groups x and z, which are not fed by primary vestibular fi- /194
bers, degeneration is more abundant than in any of the strictly vestibular nuclei. The fact that spinal afferents enter Group x is interesting from the point of view of this projection to the flocculonodular section (Brodal, Torvik, 1957). Thus for spinal impulses there is a sufficiently direct route to the phylogenetically oldest vestibular portion of the cerebellum.

It is curious that in man, evidently, the spino-vestibular fibers are organized the same as in cats.

The difference in the distribution of primary vestibular and spinal afferents inside the vestibular nuclei does not exclude the possibility of interaction between these two types of impulses.

On the whole the spinal cord does not have great capacities for exerting influence on the vestibular nuclei by means of direct connections.

Physiology

Vestibulo-Spinal Influences

Organization of the Vestibular Projection in the Spinal Cord

At the present time it is well known that the vestibular system influences both the postural and the phasic reflex activity of the spinal cord (Magnus, 1962; Fulton et al., 1930; Bach, Magoun, 1947; Gernandt, Thulin, 1953; Sprague, Chambers, 1954; Gernandt, Katsuki, Livingston, 1957; Granit, Pompeiano, Waltman, 1959; Fukuda, 1961, et al.). This influence can be conducted by many descending paths (Brodal et al., 1966). Insofar as the maintenance of postural reflexes depends chiefly on intersection of proprioceptive and vestibular activities, it is probable that there is a significant convergence of fibers conducting such activity to spinal and possibly supraspinal neurons. The effect of the vestibular stimulation on cortico-spinal (motor) activity (Gernandt, Gilman, 1960a, b; Megirian, Troth, 1964) also testify to the fact that significant interaction between these systems takes place on the spinal and supraspinal levels. Insofar as in cats the supraspinal systems have a spinal influence chiefly on the interneurons, Erulkar and coll. (1966) undertook an investigation with the aim of localizing these interneurons in the gray matter of the spinal cord. They conducted experiments on cats under nembutal anaesthesia. They stimulated the vestibular nerve, the precruciate cortex and the dorsal roots. Potentials of separate neurons in the spinal cord were registered intra- and extracellularly, and also were removed from fibers of the dorsal and ventral roots. For identification of interneurons, /195
the criteria of Frank and Fuortes (Frank, Fuortes, 1966) and of Hunt and Kuno (1959) were used. It was discovered there are strong exciting and inhibitory vestibular influences on the interneurons; moreover, interneurons receive fibers from the cortico-spinal system and from the dorsal roots, and are topographically localized at all levels of the spinal cord. Responsive stimulation of the vestibular nerve in a number of cases were long lasting, which attests to the tonic vestibular influences on the interneurons. With the maintenance of such prolonged activation, stimulation of the vestibular nerve modulates the activity of the dorsal roots acting on the presynaptic afferent fibers.

The reactions of 331 intercalory neurons of the cervical and lumbar levels of the spinal cord in response to stimulation of the vestibular nerve dorsal roots and motor cortex were registered intercellularly. Three populations of interneurons were found: those reacting only to vestibular stimulation, only to stimulation of the vestibular nerve in the dorsal roots, or to motor cortex and vestibular nerve stimulation; some of the interneurons reacted to all

three types of applied stimulation.

These three populations of neurons were distributed approximately in three columns stretching dorsal-ventrally in the spinal cord: medial, central and lateral.

It was discovered that stimulation of the vestibular nerve elicited a large potential in the dorsal root which was similar to the reflex potential of the dorsal group in its configuration. Response reactions to stimulation of the vestibular nerve were registered in the ipsilateral and contralateral roots at the level of the lumbar and sacral sections of the spinal cord. The mean latency of responses was no less than 7 msec (with weak stimulation it increased to 15 msec). The duration of responses was approximately 20-30 msec and consisted of two groups of discharges with a duration of 3-6 msec each. Responses to duration of stimulus were very sensitive. Decrease in duration to 0.1 msec lowered the amplitude of the response to 60%. A 0.4-1.0 msec duration of the stimulus was critical.

The amplitude of the dorsal reflex root with stimulation of the ramuli of the dorsal root in the same segment (increased if stimulated) was preceeded by stimulation of the ipsilateral vestibular nerve with an interval between stimuli of 35 msec. With an interval between the stimuli of 35-300 msec, the amplitude of reflector responses in the dorsal roots decreased. The given changes were accompanied by a decrease in amplitude of mono- and polysynaptic responses in the central roots. /196 If stimulation of the ramulus of the dorsal roots preceded stimulation of the vestibular nerve, responses of the ipsilateral dorsal root to stimulation of the vestibular nerve increased with the interval between stimuli of up to 35 msec, but were suppressed with an interval of 700 msec; in the contralateral dorsal roots, response to stimulation of the vestibular nerve also increased with an interval between stimuli of up to 1 sec. Suppression of responses was not discovered. Precisely the same interaction was established for two segments above and below the stimulated ramulus of the dorsal root, both ipsi- and contralaterally.

Under certain conditions, these character changes in amplitude of the dorsal and ventral root responses to stimulation of the vestibular nerve or of the dorsal root were different. After tetanization of the ipsilateral vestibular nerve (500 imp/sec in the course of 15 sec) or of the ramulus of the dorsal root, suppression of the response of the dorsal root was observed. Weakening of the response in the dorsal root with stimulation of the thin ramulus of the same root was accompanied by an increasing strengthening of response in the ventral root. With restoration of response reaction in the dorsal root, the amplitude of response in the ventral root returned to the original level. A different effect was observed with tetanization of the vestibular nerve. Immediately after cessation of tetanization, in the dorsal and ventral root responses to single stimuli of the vestibular nerve were diminished. Then during one

minute, strengthening of responses followed in the ventral roots, although responses in the dorsal roots continued to remain diminished. Later responses in both roots returned to their original amplitude.

The introduction of picrotoxin, which suppresses presynaptic inhibition (Eccles et al., 1963), elicited a pattern of changes in dorsal and ventral root responses to stimulation of the vestibular nerve similar to that with tetanization. Established differences between the point of response registration and the point of terminal endings indicate that several of the interneurons, receiving projections from the vestibulo-spinal, reticulo-spinal, cortico-spinal paths and dorsal roots, can be projected to other interneurons. However this does not at all appear to be the rule for all interneurons, since it is known that with stimulation of the vestibular nerve (Gernandt, Gilman, 1960a) of the motor cortex (Lloyd, 1941) or of the dorsal roots, discharges in ventral roots are increased. Therefore evidently interneurons can send fibers to the post-synaptic membranes of motoneurons. The data of Erulkar and coll. (1966) show that several interneurons may be projected to presynaptic terminals of the dorsal roots. The authors showed that neurons distributed in Laminae 4, 5 and 6 respond to stimulation of the vestibular nerve by multispiked discharges with a duration greater than 30 msec.

Data obtained by Erulkar and coll. show that the vestibular /197
system influences the activity of afferent fibers of the spinal cord. According to the interpretation of Eccles et al. (1961b), the vestibular system can have a presynaptic inhibitory effect on the activity of the dorsal root fibers through interneurons.

The effect of tetanic stimulation of the vestibular nerve is interesting. Before response potentials are manifested in the ventral roots, impulses from the vestibular nerve pass some intermediate stations. It is possible that the final path is the path from the interneuron to the post-synaptic surface of the motor neuron. Hyperpolarization of the interneuron axon may cause the appearance of postsynaptic potentials in the ventral roots; however, it does not explain changes in responses in the dorsal roots. These changes must be related to interneurons, upon which vestibular influences are projected. They cannot be a consequence of post-tetanic hyperpolarization of the dorsal root fibers which were not stimulated in the experiments under consideration. Suppression of responses in the dorsal roots may be connected only with an increase in depolarized activity in the interneurons, projecting on the dorsal roots, which hinders the conduction of impulses in these fibers, or with the potentiating effect in the fibers which normally elicits hyperpolarization in the dorsal roots (Mendel, Wall, 1964).

Thus interneurons at the level of the neck, thoracic and lumbar sections of the spinal cord are an important link in the coordination of impulse interaction from the vestibular system, motor cortex and dorsal roots.

Vestibular Influences on the Spinal Reflexes

In 1952 Gernandt studied the influence of adequate stimulation of labyrinths (rotation) on the impulse activity of the ventral roots innervating the posterior extremity and of motor nerves feeding flexor or extensor muscles of the posterior extremity.

With registration of activity in ipsilateral ventral roots, it proves to be the case that ampullopetal current of the endolymph increased impulse activity and ampullofugal current decreased it, but the opposite effect could not be registered. This fact allowed him to assume the possibility of bilateral influences of vestibular apparatus on the spinal cord. Actually, after sectioning the contralateral vestibular nerve only the first type of response was observed.

With section of the ipsilateral vestibular nerve the second /198
type of response was observed.

Thus these experiments show the significance of paired activity of the vestibular apparatus on both sides in influencing the activity of motoneurons.

With registration of impulse activity in n. tibiallis anterior (flexor) and n. gastrocnemius (extensor), Gernandt and Thulin (1955), during rotation of an animal, discovered that an ampullopetal current of the endolymph increases the activity of flexors and inhibits that of extensors, and inversely, an ampullofugal current activates extensors and inhibits flexors. Thus, adequate stimulation of the labyrinth has reciprocal influences on the musculature of extremities. The authors proposed that reciprocal influences were intermediated through the reticular formation, since section of the vestibulo-spinal tract did not influence the discovered effects. After unilateral section of the 8th nerve, the effects disappeared.

A reciprocal effect of the vestibular influences was also clearly demonstrated during an investigation of changes in monosynaptic reflexes in decerebrated cats under rotation (Gernandt, Thulin, 1953). Ampullopetal current of the endolymph in the labyrinth had an exciting influence on monosynaptic flexor reflexes, and ampullofugal current inhibited them. The opposite pattern was observed in the case of extensor monosynaptic reflexes. The same data were obtained from pigeons with EMG registration of reflexors and extensors of the wings (van Eyck, Gernandt, 1953). These data were found to contradict the results of direct electrical stimulation of the vestibular nuclei, by which the extensor monosynaptic reflexes were excited and the flexor ones were inhibited (Sprague et al., 1948; Thulin, 1953).

With the aim of explaining these contradictions, Gernandt and Thulin (1955b) set up experiments in which they stimulated the bulbar reticular formation and performed unilateral and bilateral

section of the 8th nerve. With stimulation of the remedial reticular formation, the amplitude of extensor monosynaptic reflexes (n. gastrocnemius) diminished and flexor monosynaptic reflexes (n. tibialis anterior) increased. After ipsilateral section of the 8th nerve, the amplitude of flexor and extensor monosynaptic reflexes lowered, and inhibitory and exciting influences with stimulation of the reticular formation were not so clearly pronounced. Still greater lowering of amplitudes of monosynaptic reflexes (in comparison with the control) was observed after sectioning the contralateral 8th nerve. These data thus show that impulses entering the reticular formation from the vestibular nuclei have an exciting influence on it. However, in the normal case these influences are completely balanced by paired activity of the vestibular nuclei, and /199
only after sectioning the 8th nerve when the balance is destroyed does the intact nerve begin to manifest its exciting influences. Consequently, the inhibitory and exciting influences become less pronounced upon stimulation of the reticular formation. Subsequent section of the other vestibular nerve completely liberates the reticular formation from vestibular influences.

Thus data obtained with adequate stimulation of the labyrinth and with electrical stimulation of the vestibular nerve are in complete correlation, i.e.: with electrical stimulation of the vestibular nuclei the same destruction of equilibrium is created which is attained by unilateral section of the 8th nerve.

Thus adequate stimulation of the semicircular canal produces reciprocal excitation or inhibition of monosynaptic extensor and flexor reflexes. What paths are responsible for the conduction of this effect? The results of the investigations of Precht and coll. (1967b) shows that some vestibular Type I, II and III neurons are projected directly into the spinal cord, i.e., the vestibulo-spinal tract and medial longitudinal bundle probably play a basic role in the realization of these effects on monosynaptic reflexes, but it is impossible to deny the possible participation of vestibular reticular paths.

Gernandt and Thulin (1955a), during stimulation of the reticular formation, discovered regions in it which have a reciprocal effect on reflexes in the ventral roots, elicited by stimulation of the nerves innervating muscular antagonists. These regions are easily discovered in the medial reticular formation and difficultly in the lateral ones. Reciprocal influences of the reticular formation could be either exciting with subsequent inhibition after cessation of stimulation, or inhibitory with subsequent increase in the value of reflexes after cessation of stimulation. The same effects were observed even with stimulation of the vestibular nuclei. It is possible to assume that different vestibular nuclei influence different regions in the reticular formation.

Vestibular Influences on α- and γ-Motoneurons

Anderson and Gernandt (1956), in experiments on decerebrated cats, studied the influence of stimulation of the vestibular nerve on the activity of α- and γ-fibers of the motor nerves. Animals were deafferentized by sectioning the dorsal roots at the L_5-S_2 level.

For γ-fibers the threshold values of stimulation strength with stimulation of the vestibular nerve were lower (by 2.5-2.9 times) than for α-fibers. With the frequency of stimulation of 1-2 imp/sec with threshold values for γ-fibers on the first stimulus, impulses could appear even in α-fibers, but on the second and subsequent ones they disappeared and could be elicited again only by increasing the force of stimulation. Response discharges in α-fibers were distinguished from those of γ-fibers by the fact that they did not increase progressively with continuous rhythmic stimulation of the vestibular nerve. /200

With stimulation of the vestibular nerve, the effect of exciting influences appears in α-fibers, the impulse frequency of which may increase to 100 imp/sec. With adequate stimulation such an increase in impulse frequency in α-fibers was never registered. Reflex discharges in α-fibers had a frequency of 20-40 and sometimes 50-80 imp/sec.

It is necessary to note that if impulses in the motor cells do not proceed along the tracts mediating vestibular influences, the frequency of their impulsation may depend upon the inhibitory feedback mechanism (Eccles, 1953), and the effect of this system cannot be differentiated from the purely exciting influences of the vestibular apparatus.

With registration of the activity in fibers of the ventral root, responses were discovered which showed that both exciting and inhibitory influences may enter the same cell. This effect was discovered with an increase in the force of stimulation (duration of stimuli was a constant 1 msec).

With an increase of stimulus higher by 1.3 and 1.7 times than the threshold stimulus, after the initial discharge a period of silence lasting up to 20 msec followed; afterwards impulse discharges were again registered. With a force of stimulus higher by 1.9, 2.2, and 2.7 than the threshold, the effect of the appearance of two discharge spindles was clearly seen. This period of silence was not connected with the central refraction ability or with lowered excitability, since the period of silence changed as a function of the force of stimulation. It also was not connected with the feedback mechanism, since after a packet of impulses following a period of silence, cessation of impulse generation in these root fibers was not observed. Evidently, this effect is connected with the

conduction of exciting and inhibitory influences along two different tracts, whereupon exciting influences are conducted faster.

With a frequency of 2-4 Hz a pair of small spikes appeared in response to each stimulus. With a frequency of 10 Hz and above, irregular large spikes appeared, the number of which continually increased with a continuation of stimulation. However, after 14 seconds the discharge frequency decreased and only large spikes were registered. In α-fibers discharges were registered even with a frequency of stimulation of 100 Hz. Although the impulse frequency was changed, the impulses never disappeared.

With a change in frequency of stimulation from 1 to 10 Hz, activity in α- and γ-fibers was registered. /201

With a frequency of stimulation of 20 Hz, activity in the γ-fibers was completely suppressed. For 5 seconds after cessation of stimulation the impulse frequency markedly increased. This increase in activity indicates the inhibitory component of vestibular influences since the effect cannot be associated with fatigue: discharges appeared immediately after cessation of stimulation. Stimulation of proprioceptors suppressed the effect of stimulation of the vestibular nerves in α- and γ-fibers.

Thus, tonic activity in γ-afferents was connected with a moderate current of impulses from the 8th nerve. Activity of α-fibers "restrained" the activity in the γ-fibers through return collaterals to the cells of the ventral column which give rise to γ-fibers. Thus, initially, stimulation of the vestibular nerves increases the activity of γ-fibers, then of α-fibers which, finally, elicit muscular contraction. Furthermore, inhibition probably develops according to the type of feedback, i.e., regulation of muscular contraction is controlled by the muscles.

With the study of γ-activity during adequate stimulation of the vestibular apparatus (angular acceleration), Totsuka and coll. (1963) showed reciprocal and nonreciprocal influences of the latter on the system of γ-fibers. Nonreciprocal influences were discovered with stop stimuli and were expressed by an increase of activity in γ-fibers independent of the direction of rotation. However, with counter-clockwise rotation activity was increased in the α-fibers of the left flexors and right extensors and was inhibited in γ-fibers of antagonist muscles. The opposite development was observed with clockwise rotation. An increase in extensor activity was found to be linearly dependent upon the amount of acceleration. The authors assume that direct vestibular influences on α-fibers are controlled by the system of γ-fibers.

Vestibulo-spinal influences on α-motoneurons were studied by A.I. Shapovalov and coll. (1966) in cats immobilized by flaxedil. They stimulated the vestibular apparatus (they conducted the electrode through the round window), and in several experiments they

stimulated (with bipolar electrodes) Deiter's nucleus. With investigation of 146 lumbar α-motoneurons in 80 cells, SPSP's were registered; in 42 cells, IPSP; and in 24 cells the reaction was of mixed nature. The mixed character of post-synaptic responses was more clearly manifested with the use of rhythmic stimulation at various frequencies. Vestibular stimuli, as a rule, elicited SPSP in extensors and IPSP in flexor motor neurons. Action potentials were generated under the influence of single or rhythmic stimuli applied to the round window. Sometimes several stimuli were required (from 2-3 to 10-12) to produce the appearance of a clearly distinct SPSP, which may attain critical level for generation of single and group discharge.

SPSP arising under the influence of vestibular stimulation can /202 be separated into 2 or 3 components, the first of which arose with a very short latent period (minimum value 3.5-5.0 msec) and had a very short temporal passage, similar to the duration of SPSP, elicited by stimulation of muscular afferents of Group 1A. However, the amplitude of these short latent components is very small (-2-3 mV). A more delayed wave of post-synaptic depolarization began immediately after the first component, had a prolonged temporal flow, could attain an amplitude of 6-8 mV and undoubtedly represented the result of post-synaptic excitation.

The very shortest latent period of appearance of SPSP in lumbar motoneurons, with electrical stimulation of Deiter's nucleus, equalled less than 3-4 msec. The focal response, registered by a microelectrode located in the region corresponding to the topography of the fibers of the vestibulo-spinal tract, arose 0.5 to 0.3 msec earlier than the beginning of the short latent component of SPSP. This circumstance allowed the authors to consider the short latent component as a result of monosynaptic excitation of motoneurons by vestibulo-spinal impulses.

In the course of rhythmic stimulation monosynaptic vestibulospinal SPSP exhibited an appreciable potential.

IPSP could be elicited both by single and by rhythmic stimulation. IPSP was elicited by single stimulations at an amplitude of 1-2 mV (more rarely 5-6 mV) and appeared with latent period not less than 6-7 msec, which indicates the presence of supplementary synaptic delays along the path to the motoneurons. In a significant number of cases IPSP arose only with tetanic stimulation. Stimulation at a frequency of 200-300 times per second appeared to be effective, enabling these values of post-synaptic hyperpolarization to attain 10-12 mV.

Artificial displacements of transmembrane potential differences with the aid of passing an electrical current through a cell led to regular changes in IPSP elicited by vestibular stimulation: depolarization increased and hyperpolarization decreased, and with the passage of a sufficiently strong current distorted vestibulo-

spinal IPSP's, converting them to depolarized ones. Reversal of IPSP began under the influence of a hyperpolarizing current with a strength of $12\text{-}16 \cdot 10^{-8}$A. These experiments established a complete similarity between IPSP elicited by stimulation of nerves of the lower extremities and the vestibular apparatus, and convincingly testified to post-synaptic origin.

The action of a polarizing current on SPSP, elicited by vestibular stimulation, was not as monotypic. In a large portion hyperpolarization and depolarization did not influence the SPSP amplitude. This was the case in 24 of 37 motoneurons. In some of the cells depolarization even increased somewhat and hyperpolarization diminished the SPSP amplitude. Such an effect was especially clearly manifested in the short latent SPSP, considered as a result of monosynaptic vestibulo-spinal excitation. In these same cells hyperpolarization increased and depolarization decreased the polysynaptic SPSP elicited by afferent stimulation. The same results were obtained even with vestibulo-spinal excitation. /203

The data obtained by the authors evidence the possibility of monosynaptic activation of lumbar motoneurons by vestibulo-spinal impulses. Insofar as morphological investigations (Nyberg-Hanson, Mascitti, 1964) could not reveal vestibulo-spinal endings of motoneurons, the authors assumed that synapses formed by endings of the vestibulo-spinal tract fibers and by motoneurons are localized primarily in the region of dendrites of the latter. Data from experiments investigating the influence of transmembranal polarization in a majority of vestibulo-spinal SPSP confirm this assumption. Insofar as in the same cells polarization noticeably changed the polysynaptic SPSP and IPSP, the authors concluded that the obtained results are not an artifact connected with injury to the cells by the microelectrode. The authors assumed that the fact under consideration is related to the large distance between the microelectrode introduced into the soma and with activated synapses, which may take place with dendritic distribution of the latter. At the same time the clear and regular change in vestibulo-spinal IPSP under the influence of polarization, in the opinion of the authors, attests to the distribution of inhibitory synapsis in the region of the soma or portions of dendrites near it.

Sasaki et al. (1962) studied the influence of electrical stimulation of Deiter's nucleus on the spinal monosynaptic reflexes in cats. The authors established that electrical stimulation of Deiter's nucleus had an exciting effect on flexor monosynaptic reflexes (stimulation of n. tibialis). Exciting influences may be separated into two components: the initial exciting influences having short latency (several msec) and the late exciting influences with a latency of 15-20 msec and duration greater than 30 msec. With intracellular registration in the lumbar α-motoneurons during stimulation of Deiter's nucleus, early and late depolarized PSP's were discovered. The early PSP's had a latency of about 10 msec and were of short duration; the late PSP's had a latency of 15-20 msec or larger and

had a significant duration, up to 100 msec.

Both the early and late SPSP could generate spikes. However, for the later SPSP the critical level for the generation of a spike was equal to 20 mV and was significantly higher than that for the early ones. Stimulation of Deiter's nucleus had an insignificant /204
effect on PSP of the flexor motoneurons. Sasaki and Tanaka (1964) consider that early SPSP may be conditioned by physical influences and be conducted along specific paths, and the later by tonic influences and be conducted along nonspecific paths. These assumptions of Sasaki and coll. (1962, 1964) are confirmed by the data of Pompeiano and Morrison (1966), who studied the influence of the destruction of the medial and descending vestibular nuclei of spinal reflexes. It was shown that heteronymic monosynaptic reflexes, as well as polysynaptic reflexes, are completely suppressed during the phase of desynchronized sleep. Insofar as suppression of the reflexes was observed during the entire phase of desynchronized sleep, the authors attribute this inhibition to the tonic period. The homonymic monosynaptic reflexes, although depressed, are not suppressed, and even disappear during rapid eye movements. The authors posit that such strong suppression during short intervals of time is conditioned by physical inhibition.

After destruction of the medial and descending nuclei, phase depression of monosynaptic reflexes was not observed. Destruction of these nuclei did not influence tonic inhibition.

Morrison and Pompeiano (1965b) showed that tonic inhibition is related to prosynaptic structures, and phase inhibition is connected with presynaptic structures. According to the data of Carpenter and coll. (1966) on desynchronized sleep, during rapid eye motions depolarization of the Group I fibers develops, as a consequence of which the monosynaptic reflex is blocked. Pompeiano and Morrison (1966) established that these influences from the medial and descending nuclei are bilateral and are mediated by conduction through the medial longitudinal bundle, and tonic inhibitory influences are conducted along the reticular spinal tract.

Sinovestibular Influences

In experiments on cats under chloralose urathane and nembutal anaesthesia, Wilson et al. (1966) studied response reactions of the neurons of Deiter's nucleus to stimulation of the following ipsilateral nerve trunks: n. suralis (SUR); n. gastrocnemius + soleus (GS); n. plantaris (PL); n. flexor digitorum longus + n. tibialis posterior (FDL); n. plantar (PLANT); n. peronealis communis (CP) and the nerve of the popliteal tendon (HS), from which in several experiments they separated n. biceps posterior semitendinosus (BST); n. biceps anterior (BA); n. semimembranosus (SM); in CP they separated n. peronealis superficialis (SP); n. tibialis anterior + n. /205
extensor digitorum longus (TA + EL); contralaterally they separated HS, SUR, CP, and PLANT. With the aid of antidromic activation of

the vestibulo-spinal tract, 163 neurons of Deiter's nucleus were identified; 149 of these were activated with stimulation at the level of L_3-L_4. These units were designated as L-units. Some of the neurons were activated only with stimulation of the cervical segments or C-units. This group also included neurons penetrating as far as the thoracic and superior lumbar sections of the spinal cord.

It was discovered that L-cells are more numerous in the caudal portion of the nucleus than in the rostral portion. These cells were located in the ventral portion of the nucleus. Spontaneously active cells were found more frequently in the caudal portions of the nucleus.

With stimulation of the vestibular nerve, 31 of 61 C-cells (51%) and 18 of 80 L-cells (22%) were activated. Among the L-cells, 11 had axons with a speed of conduction of more than 80 m/sec, and 8 more than 100 m/sec, i.e., axons probably terminated in large cells, which contradicts the known anatomical data (Brodal et al., 1966). Between the rostral and caudal portions of the nucleus there were no differences during activation of the labyrinth, but between the dorsal and ventral portions such a difference was noted. In the dorsal portion of the nucleus almost no monosynaptically activated cells were found. Monosynaptic responses were most often registered in cells silent at rest. Thus, L-cells were numerous in the region not having entrance from the labyrinth (Wilson et al., 1967).

With stimulation of mixed or cutaneous nerves (CP, PLANT, SUR, SP, and FDL), the rhythmicity of neurons of Deiter's nucleus almost always increased. With stimulation at a frequency of 1 imp/sec, rhythmicity could be increased by 50-100% in the course of 100 msec. Stimulation of all the enumerated nerves gave the same effect. With stimulation of the nerves BST, SM, BA, TA + EL, PL and GS, a very weak increase in rhythmic activity was discovered (in only 5 units of 39 did the rhythmicity increase by more than 20%).

The effect increased with stimulation by triple stimuli during 380 sec.

In mixed nerves with such stimulation the effect was not increased so strongly. This evidently is connected with the fact that the paths from the muscular nerves demand greater temporal summation.

If cells of Deiter's nucleus reacted with ipsilateral stimulation of the nerves then they responded even to contralateral stimulation, but the reaction was weaker.

Fredrickson and coll. (1966) discovered preservation of contralateral influences with deep barbiturate anaesthesia. These authors assume that intracommissural fibers in the vestibular nuclei play an important role in the contralateral effect of activation of vestibular nuclei. With stimulation of the ipsilateral superficial radial nerve, 26 of 36 L-neurons were activated, whereupon they /206

reacted noticeably more strongly than with stimulation of mixed or cutaneous nerves of the posterior extremity (Wilson et al., 1966).

Such an extensive convergence of L-cells of the lateral vestibular nucleus in the afferent nerves of both rear extremities and the forward ones were characteristic for all cells.

Thresholds of excitability were defined by Wilson and coll. (1966) for 21 cells. The value T, i.e., the force of stimulation of nerve trunks with which changes in activity in dorsal roots were noted, was taken as a unit of measurement. Activation of L-cells with stimulation of the ipsilateral cutaneous or mixed nerves was within the bounds of 1.3-1.4 T. Thresholds of activation with stimulation of muscle nerves were significantly higher than 6, 8 and 9T. Consequently the low threshold with stimulation of mixed nerves was not conditioned by fibers innervating muscles. With contralateral stimulation the thresholds were the same. With stimulation by a triple stimuli the thresholds were lowered: muscle nerves not activating neurons of Deiter's nucleus with single stimulation began to activate with a force of 6-10 T; sometimes thresholds were 4-5 T and lower. Lowering of a threshold with stimulation by triple stimuli indicates the importance of temporal summation. Thresholds of C-cells is the same as for L-cells. Wilson and coll. (1966) observed that stimulation of the L_3-L_4 level elicited not only antidromic activation but also later synaptic activation of the cells.

It is possible to assume that with such stimulation the stimuli are propagated along the waves of the dorsal-lateral portion of the brain (vestibulo-spinal tract is distributed ventrally).

However, it is more probable that the effect is connected with the activation of fibers in the ventral quadrant. Such an assumption admits that not only straight spinal vestibular fibers are included in the effect but also that ascending ones are included in the composition of the spino-cerebellar tract, located in the dorsal portion of the lateral white substance. The bilateral effect confirms the inclusion of ventral or ventral-lateral paths. With one exception, the fibers distributed in the dorsal portion of the ventral-lateral white matter are activated only by ipsilateral nerves, while those which are located in the ventral-lateral white matter are activated both by ipsi- and contralateral stimulation.

The experiments of Wilson and coll. (1966, 1967) are similar to experiments of Pompeiano and Cotti (1959) which also indicated that antidromic activation of peripheral nerves elicits an exciting effect in vestibular neurons of the rear extremity of Deiter's nucleus. However, the latter authors did not remove the cerebellum. Wilson and coll. (1966) demonstrated the direct paths conducting /207
exciting and inhibitory influences to Deiter's nucleus. The inhibitory effect is especially important, since it could be assumed that inhibitory influences were intermediated through the cerebellum.

Pompeiano and Cotti (1959) and Fredrickson and coll. (1966b) discovered that flexion of an extremity in cats, percussion along the tendon (but not pressure on the muscles), stroking against the fur and pulling the whiskers can cause activation of the cells of Deiter's nucleus. Thus perception of motion, weight and position doubtless is connected with the activation of the lateral Deiter's nucleus. It is necessary to emphasize that Deiter's nucleus is activated only through the spino-vestibular tract; in the ventral-lateral white matter fibers of the spinal-reticular and spinal-olivar tract pass, which activate the nuclei through the reticular formation, the olivo-cerebellar fibers also give contralaterals to the vestibular nuclei.

The data of Precht et al. (1967) testifies to the possibility of such activation of the vestibular nuclei. The authors studied the activation of the vestibular neurons of three types with stimulation of tr. vestibulo-spinalis and the medial longitudinal bundle. They separated the neurons of the vestibular nuclei into two groups: those reacting antidromically (the latency of responses of these neurons fluctuated within a 0.5 msec range, and they responded to paired stimuli with an interval between the stimuli of 2 msec and less); and neurons reacting transynaptically (the shortest latency of responses of these neurons equals 2.2 msec and fluctuated significantly, and the neurons did not respond to stimulation by paired stimuli).

Of 65 Type I neurons localized in the superior and medial nuclei only one was excited antidromically by the stimulation of the medial longitudinal bundle, 4 were excited transynaptically, and in 60 there was no reaction. Therefore the number of Type I neurons projecting to the spinal cord is not great.

Of 30 Type II neurons chiefly located in the medial nucleus, 6 were activated antidromically and 24 transynaptically.

Of 18 Type III neurons, 14 were excited antidromically. In half of these neurons the threshold was lower with stimulation of the medial longitudinal bundle. Histological control showed that these neurons were distributed in the medial vestibular nucleus.

Many neurons reacting antidromically to stimulation of the medial longitudinal bundle were not activated with rotation. The authors assume that they are not connected with horizontal semicircular canals.

The data in this chapter show that the vestibular apparatus has powerful influences on the spinal cord. These influences are intermediated through the vestibulo-spinal tract, the reticulo-spinal and the medial longitudinal bundle. Along the vestibulo-spinal tract both mono- and polysynaptically exciting vestibular influences are /208
transmitted. Along the reticulo-spinal tract are transmitted both exciting and inhibitory influences. The medial longitudinal bundle

intermediates the conduction of exciting vestibular influences. The fibers of the medial longitudinal bundle are both intersecting and nonintersecting; the fibers of the vestibulo-spinal tract are non-intersecting, although they may send collaterals for innervation of the contralateral motor pool. Through the commissural fibers along the reticulo-spinal tract are conducted crossing and noncrossing vestibular influences. Influences conducted along all three tracts basically are projected onto interneurons, although it is possible that there are monosynaptic paths even to the motor neurons. Vestibular influences on motoneurons and spinal reflexes may be divided into phasic and tonic.

Interneurons onto which vestibular influences are projected may in turn be projected onto fibers of the dorsal roots entering the spinal cord. At the same time, impulses entering the spinal cord along the dorsal roots change the activity of the lateral vestibular nuclei.

Modifying the activity of the fibers of the dorsal roots, the vestibular system thereby modifies the activity of the neurons giving rise to the vestibulo-spinal tract. This feedback system is interesting by the fact that it permits us to assume that even the activity of other ascending sensory systems may be modified by vestibular stimulation.

CHAPTER VI

CONNECTIONS OF THE LABYRINTH WITH THE CEREBELLUM

Morphology

Vestibulo-Cerebellar Connections. A detailed study of the distribution of primary vestibular fibers in the cerebellum was conducted in cats using the Naut-Gigax and Gliss methods (Brodal, Høivik, 1964). /209

According to these data, numerous original vestibular fibers to the cerebellum pass through the superior vestibular nucleus or above it. Dorsal of the vestibular nucleus the fibers are formed in bundles and are distributed flabellately in the dorsal direction. Insofar as according to the data of Lorente de No (1933a) the superior nucleus is connected with the semicircular canal, it is possible to consider that direct influences on the cerebellum originate in the semicircular canals.

The majority of primary vestibular fibers is distributed in the ipsilateral half of the nodulus, in the ipsilateral flocculus, in the proximal and ventral portions of the uvula and the ventral perifloccullus.

A small number of degenerated fibers is found in the lingula and the dorsal perifloccullus. In all these regions the fibers entered the granular layer of the white matter. In the uvula the intensity of degeneration is narrowed to the surface from the fissura posterior lateralis to the fissura secunda. In lamina *b* (according to Larsell, 1953) there is a small degeneration and in lamina *a* almost no degeneration is detected.

In corresponding regions of the contralateral half of the cerebellum there is a very small number of degenerated fibers. The indicated degenerated fibers pass through the cerebellum nuclei. Tree-like branches of the primary vestibular fibers were discovered around several cells of the parrocellular portion of the nuc. dentatus. Between the cells of this region degeneration of the thin fibers, passing in various directions are found. Thick fibers pass medial-laterally and appear on the lateral side of the nuc. dentatus. /210

In the medial nucleus (nuc. fastigii) of the cerebellum the authors, as opposed to Carpenter (1960), did not discover degeneration of primary fibers. Degeneration did not appear even in nuc. interpositus. Several synaptic contacts were able to be shown in Group V cells (Brodal, Pompeiano, 1957).

The degeneration of primary vestibular fibers discovered in the granular layer of the white matter is treated by the authors as the terminals of mossy fibers. They are similar to the terminals of the spinal cerebelli fibers in the forward portion of the cerebellum. The terminals for the primary vestibular fibers terminate even as scansorial fibers. In the molecular layer no degeneration was found; however, degenerated fibers are found even in the immediate neighborhood to Purkinje's cells.

These data show that the distribution of primary vestibular fibers encompasses a zone greater than the flocculo-nocular portion of the cerebellum which is considered easily as the vestibular cerebellum. Portions of the uvula, ventral and dorsal periflocculus and a small portion of the nuc. dentatus are usually included in the vestibular cerebellum.

It follows to note that there is a point of view that the vestibular cerebellum in the process of embryogenesis originates from cells of the vestibular nuclei. However Rudeberg (1964), studying development of the cerebellum in baby chicks in the extirpated zone of the vestibular neuromere, showed that all the sections of the cerebellum were developed normally, and it is doubtful that the cerebellum develops as a consequence of migration of cells from the vestibular nuclei.

Fibers from the vestibular nuclei to the cerebellum were traced by Dow (1936) according to Markey's method, which indicated that they terminate in the flocculus, nodulus, uvula, and nuc. fastigii chiefly ipsilaterally. The study by the method of retrograde degeneration (the modified Gudden method) showed that these fibers originate from specific portions of the medial and descending nuclei (Brodal, Torvik, 1957). The preparatory observations of Grant (1962) showed that the endings of these fibers are mossy. Fibers from Deiter's nucleus to the cerebellum were not found. Cell groups *x* and *f* also send fibers to the cerebellum. Brodal (1964) notes that these regions of the vestibular nuclei which are projected onto the cerebellum do not receive primary vestibular fibers, or that if they do it is only in a limited number. Therefore the question of whether secondary vestibular fibers intermediate transmission of impulses from the labyrinth to the cerebellum (its flocculo-nodular portion) remains open.

Brodal and Drabløs (1963) discovered that the mossy terminals in the vestibular zone of the cortex of the cerebellum differ from the same terminal in other zones of the cortex. These differences /211 are discovered in Gliss slices and on Golgi preparations. Endings

of the nodular type in the vestibular zone are more compact and are richer in patches than the mossy terminals of the classical type. However, Brodal (1964) notes that even if the "vestibular cerebellum" is larger than was supposed up to this time, it occupies only a small portion of the entire surface of the cerebellum. The vestibular apparatus does not have direct connections with those regions of the cerebellum which feed the vestibular nuclei: namely the vermis cerebelli and the nuc. fastigii.

Cerebello-Vestibular Connections. The direct cerebello-vestibular tract was studied by Jansen and Walberg (1961). The fibers from the zone of the anterior extremity of the forward portion of the cerebellum terminated in the zone of the anterior extremity of Deiter's nucleus. There is exactly the same pattern in the projection of the zone of the posterior extremity. However the endings of the direct cerebello-vestibular fibers do not completely cover the zone of the anterior and posterior extremities of Deiter's nucleus. The region of the endings is limited by the dorsal half of the nucleus, while in the ventral half degeneration is not observed.

Certain regions of the fastigial nucleus are also connected with zones of the anterior and posterior extremities of Deiter's nucleus. The rostral portion of the nuc. fastigii sends fibers to the dorsal portions of the lateral vestibular nucleus.

Thus, the paths from the cerebellum to the lateral Deiter's nucleus, from which, by means of the vestibulo-spinal tract, impulses are conducted to various levels of the spinal cord, are organized somatotypically. Somatotypical paths conducting the impulses influencing muscle tone, as Brodal proposes (1964), exist even from the anterior and posterior vermis. The cerebellar vestigio-reticular path, although involved in the conduction of impulses from the cerebellum, does not have somatotypical organization.

Direct cerebellar cortical vestibular fibers to the descending nucleus are bounded by its dorsal portion (Walberg, Jansen, 1961). Fibers from the nuc. fastigii terminate in all 4 chief nuclei and in the cell groups *x* and *f*. Fibers from nuc. fastigii to the superior vestibular nucleus terminate, scattered in its ventral portion, while primary vestibular fibers terminate in the central portion of this nucleus.

Fibers from the anterior and posterior vermis, both the direct ones and those synaptically interrupted in the nuc. fastigii, proceed from the region of the cerebellum, called spino-vestibular, insofar as it receives a basic mass of impulses from the spinal cord. However even the flocculo-nodular portion of the cerebellum influences the vestibular nuclei. Dow (1936, 1938) showed by Markey's method that the nodulus sends fibers to all 4 nuclei, while projections from the flocculus is limited by the superior and lateral nuclei. These connections were not studied by the method of impregnation with silver, and therefore there is no possibility of showing their

projection to be further differentiated. However it is clear that the "spinal" regions of the cerebellum have more possibilities /212
to show influence on the vestibular nuclei than the "vestibular" regions.

Physiology

Vestibulo-Cerebellar Influences

Price and Spiegel (1937), registering electrical activity of the cerebellum with rotation of animals, discovered an increase in spontaneous activity in the vestibular region of the cerebellar cortex.

Dow (1939), studying elicited potentials in various sections of the cerebellum with electrical stimulation of the vestibular nerve, observed responses in the flocculo-nodular portion, the ovula (9th lobulus), the lingula (5th lobulus) and nuc. fastigii. Latency of responses was on the order of 4.5 msec. In one experiment a response of 0.6 msec was registered after the beginning of stimulation, and the authors connected it with conduction along primary vestibular fibers to the cerebellum.

Chan Sian-Tung and P. G. Kostyuk (1960) registered discharges of separate neurons of the cerebellum of toads elicited by stimulation of vestibular nerves. The authors noted that stimulation of the 8th nerve elicited neuron discharges both on the ipsi- and contralateral side in all portions of the cerebral cortex, although they were most easily discovered in regions located at a distance of 0.5 mm to both sides from the central line. Histological control showed that reacting neurons were situated at a depth corresponding to the layer of Purkinje's cells. The latent period of cerebellum responses varied from 6 to 50 msec. On the basis of 253 measurements, the variation curve of latent periods had two maxima: the primary maximum was approximately 22 msec and the secondary was approximately 12 msec. The authors assumed that responses with a longer latent period were connected to impulses passing through the vestibular nuclei, and those with a smaller latent period to conduction along the direct vestibulo-cerebellar fibers. Very interesting are the observations of Linas et al. (1967) of the frog. The authors showed that primary vestibular fibers to the cerebellum (to the auricular portion of the caudal-lateral quadrant) elicite activation of Purkinje's cells according to the systems of scansorial and mossy fibers. The latency of responses of Purkinje's cells with activation by scansorial fibers equal 0.8 to 1.6 msec (monosynaptic responses), and with activation of mossy fibers equal up to 16 msec (polysynaptic responses). The authors supposed that primary afferent fibers provide kinetic influences to the cerebellum with the aid of scan- /213
sorial, tonic with the aid of mossy fibers.

Chan Sian-Tung and P. G. Kostyuk (1960), as well as activation of rhythmicity of cerebellum neurons of the toad with vestibular

stimulation even discovered inhibition of spontaneous discharges of neurons.

Weber and Steiner (1965) with caloric tests and galvanization of labyrinths in cats and rabbits noted depression in the neurons of the cerebellar cortex as well as an increase of rhythmic activity.

In experiments on cats, Granit and Phillips (1956) showed that spontaneous discharges elicited by direct stimulation of the cerebellum could be controlled by stimulation of nuc. fastigii, which receives abundant vestibular afferentation.

Inhibition of spontaneous discharges of definite cerebellar neurons by vestibular impulses is probably one of the mechanisms lying at the basis of coordinated posture control (Chan Sian-Tung and Kostyuk, 1960).

Vestibular influences on nuc. fastigii were studied by Arduini and Pompeiano (1957). In decerebrated cats they registered spike activity of nuc. fastigii neurons with polarization of the labyrinth. They investigated only the rostral third of the nucleus under the influence of the vermis of the ipsilateral anterior portion. It was discovered that galvanic cathode stimulation of any labyrinth could influence units reinforcing activity as well as units responding by inhibition to stimulation of the vermis of the anterior portion with a constant current. Thus, monopolar cathode polarization of the ipsilateral labyrinth (0.1 - 0.8 mA) led to reinforcement of the discharge rhythm of practically all units in the rostral (rostral-medial and rostral-lateral) portions of the nuc. fastigii. Stimulation of the contralateral labyrinth was not effective for approximately half the units, while in other units spike activity was strengthened. Inhibitory responses were observed only in a few other cases. Approximately half of the units on which polarization of the cerebellum had no effect responded to stimulation of the ipsilateral labyrinth. Thus vestibulo-fastigial fibers are distributed bilaterally.

Vestibular impulses arriving at the rostral portion of nuc. fastigii can reach it only along vestibulo-fastigial fibers or along the path passing through the cortex of the cerebellum. There are no physiological data on this question, but anatomical data acknowledge the existence of these two paths.

A study of the character of labyrinth influences on the cerebellum through primary vestibular fibers as well as secondary ones demands still further development and evidently will be an object of investigations in the near future.

Cerebello-Vestibular Influences /214

In numerous works the inhibition of muscle tone with stimulation of the cerebellum was studied (cf. Brookhart, 1959; Dow, Moruzzi,

1958). However, opinions on the question of the paths and sources of these inhibitory influences were contradictory. Several authors assume that inhibitory influences were intermediated through the bulbar centers; others that they arrived directly at the spinal cord (cf. Brookhart, 1959).

Electrophysiological investigations discovered that with stimulation of the anterior vermis by galvanization or impulse current, Deiter's nucleus units can be registered reacting only to inhibition or excitation (de Vito et al., 1956; Pompeiano, Cotti, 1959).

A detailed analysis of the influences of the cerebellum on the lateral Deiter's nucleus with the aid of intracellular registration of potentials of the neurons of this nucleus in cats under nembutal anaesthesia were conducted by Ito and Yoshida (1964, 1966). Identification of neurons of Deiter's nucleus were made by antidromic stimulation of the vestibular tract. The 3rd, 4th and 5th lobulus (according to Larcel) of the cortex of the cerebellum were stimulated with concentric electrodes, and in certain experiments,the white substance near the nuc. fastigii. Entrance to the neurons of the vestibular nuclei was accomplished through the side of the neck.

Seventy intracellular removals of charge were registered. The rest potential of neurons of Deiter's nucleus equaled 40-60 mV. With stimulation of the ipsilateral anterior portion of the cerebellum, hyperpolarization of the cellular potential was often registered (Fig. 64a) in neurons of Deiter's nucleus with a current of 1-5 V. With duration of rectangular voltage impulses of 0.2 msec and an amplitude of 10 V, latency of hyperpolarization was less than 2 msec with stimulation of the 3rd or 4th lobulus of 52 of 55 cells; with stimulation of the 5th lobulus in 23 of 24 cells; and with stimulation of the zone neighboring the nuc. fastagii in all 9 registered cells. The value of hyperpolarization equalled 5-10 mV. With comparatively small stimuli the hyperpolarized wave had a simple configuration. It developed in 1 msec after the beginning of stimulation, lasted an average of 1.4 msec and decreased exponentially with a half-value period of 3.3 msec. In the majority of cases the hyperpolarized wave had a complex shape with a supplementary wave of hyperpolarization (Fig. 64 e-g) delayed by 2-8 msec. With comparatively large amplitudes of stimuli the usual duration of hyperpolarization could be equated to some tenths of milliseconds (Fig. 64h). After a hyperpolarization wave a depolarization wave of low amplitude usually follows. The normal duration of changes of membrane potential was within hundreds of milliseconds.

Hyperpolarization of the membrane was identified as IPSP of /215
the same nature as in spinal motoneurons and other nerve cells (Eccles, 1966). With transmission through a microelectrode of a current with a force of 1 to $3 \cdot 16^{-8}$ A, and also with iontophoretic introduction of Cl^- inside the cell, hyperpolarization decreased and could be transferred to depolarization (Fig. 64j). The inhibitory effect was observed even in cases when the cell possessed

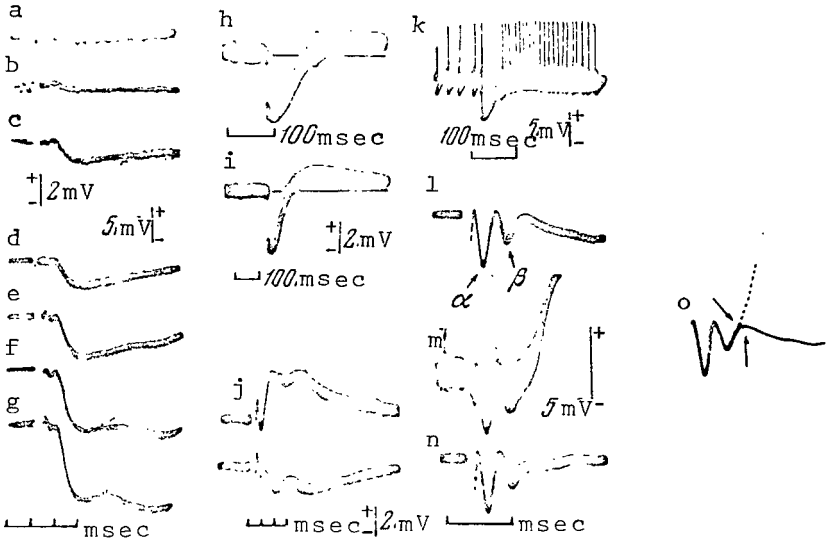

Fig. 64. IPSP in Neurons of Deiter's Nucleus with Stimulation of the Ipsilateral Forward Portion of the Cortex of the Cerebellum of a Cat (Registration of 5 Different Cells). (a-g) Stimulation of the Cortex of the Vermis or of the 4th Lobulus (Amount of Stimuli Respectively 1.9, 2.1, 3.2, 5.0, 10.0, 20.0, 30.0 V; Calibration for a-c: 2 mV; for d-g: 5 mV); (h,i) Registration with Slow Speed Development (the Base Line is Indicated) (j). Lower IPSP Recording Elicited by Stimulation of the Lobulus, Upper- with Transmission Through Microelectrode of a Hyperpolarized Current ($3 \cdot 10^{-8}$ A); (k) Suppression and Excitation of Spontaneous Discharges with Stimulation of the Forward Portion of the Cortex of the Cerebellum; (l) Initial Portion of IPSP Elicited by Stimulation of the Forward Portion of the Cerebellum; (m) After Transmission of Hyperpolarized Current ($2 \cdot 10^{-8}$ A); (n) Extracellular Registration Immediately After Withdrawal of the Electrode from the Cell; (o) Superposition of Recordings l (Solid Line) and m (Dotted Line). Time Constant 200 msec, With the Exception of h - i, and k - l Where Registration Was Produced With the Aid of a Constant Current Amplifier. Duration of Stimulus 0.2 msec. Recording Obtained by the Superposition of 10-40 Ray Sweeps (Ito et al., 1966a).

spontaneous activity. After the period of depression of spike discharges an increase in the number of spikes was noted corresponding to the phase of depolarization (Fig. 64k). With stimulation of the cerebellum (3rd and anterior portion of the 4th lobulus) on recordings with a high speed of scanning before the development of IPSP, two negative spike-like deflections of the ray were registered called α and β waves (Fig. 64l). Hyperpolarized current transmitted intercellularly through the microelectrode (Fig. 64m) did /216

not influence these waves. They were registered even extracellularly. Therefore they appear, in the opinion of the authors, as focal potentials. The beginning of IPSP was defined as a superposition of recordings l and m (arrow on Fig. 64o). In 39 of 49 registered neurons IPSP arose immediately after the β waves (Fig. 64 l). These IPSP were called early IPSP in distinction to delayed IPSP. On the average, latency of early IPSP corresponds to 1.06 ± 0.11 msec.

Latency of IPSP depended upon the location of the stimulating electrodes. The average value of latency of early IPSP of 19 cells with stimulation of the 5th lobulus equalled 1.23 ± 0.1 msec, i.e., it was significantly greater than with stimulation of the 3rd and 4th lobuli. If the stimulating electrodes were introduced into the white matter, then the character responses were the same as the stimulation of the 3rd and 4th lobuli but with significantly less latency. In 9 cells with stimulation of the region near the nuc. fastigii latency totalled 0.86 ± 0.04 msec.

Extrapolating, it is possible to assert that with stimulation by an electrode located in the region of the nuc. fastigii, latency equals around 0.5 msec, i.e., it is of the same order as that of latency of one synaptic delay in the spinal cord. Consequently IPSP in neurons of Deiter's nucleus arises from impulses which pass through one synapsis.

The authors established that the speed of conduction of impulses for early IPSP was comparatively slow and equal to 15 - 20 msec. Although with stimulation of the cerebellum in neurons of Deiter's nucleus IPSP predominated, SPSP was also registered. Figure 65a-f indicated depolarized potentials arising with a small value of the stimulus. A stimulus of 15 volts transformed IPSP into SPSP. With stimulation of the 3rd and 4th lobuli with a stimulus of 30 V in two cells, SPSP's with a shortened latency arose. With stimulation of the 5th lobulus SPSP was registered in one cell. Even if IPSP were superimposed on SPSP, the beginning of the latter could be discerned in comparison with the intracellular and extracellular registrations (Fig. 65e,f).

Latency of early SPSP with stimulation of the 3rd and 4th lobuli for 7 cells was equal to 0.91 ± 0.15 msec on the average. The authors consider that early SPSP was elicited monosynaptically with a speed of impulse conduction higher than 15-20 m/sec for inhibitory fibers.

Figure 64l and 65c show that stimulation of the cerebellum elicited negative spike-like focal potentials in Deiter's nucleus. These potentials evidently were elicited by presynaptic impulses, insofar as they were discovered on recordings of intracellular removals of charge up to the appearance of IPSP and SPSP (Fig. 64o and Fig. 65f).

Upon conducting an electrode through Deiter's nucleus, the

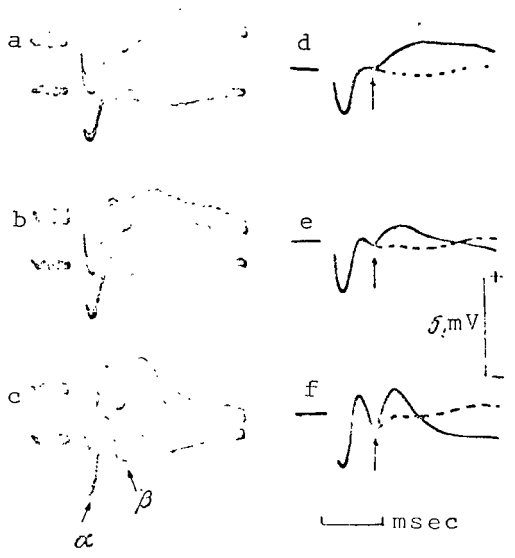

Fig. 65. SPSP in Neurons of Deiter's Nucleus with Stimulation of the Forward Portion of the Cortex of the Cerebellum of a Cat. (a-c, g-h and i) Registrations from Various Cells; (a-c) Stimulation of the Medial Portions of a Cortex of the 3rd Lobulus (Duration of Stimulus: 0.08 msec), Amplitude: (a) 12 V; (b) 15 V; (c) 30 V. The Upper Recordings Changes of Intracellular Potentials. The Lower Focal Potentials Registered Extracellularly Immediately After Withdrawal of the Electrode from the Cell. Spike-like Focal Potentials α and β are Shown in c, d, e, f. Recordings of Intracellular Potentials (Solid Line) and Extracellular (Dotted Line) are Registered in a, b, c, (Ito et al., 1966a). /217

focal potentials changed their configuration. In Figure 66, using the method of superposed registration along two tracts, it is demonstrated that this change of configuration of potentials is connected with the conversion of a β-wave from a primarily negative to a primarily positive wave while an α-wave does not undergo changes. Thus the initial point of the negative phase of an α wave, as is shown in Figure 66a and b by vertical arrows, is gradually displaced. These changes in potentials are explainable if we assume that impulses eliciting the appearance of β waves in Deiter's nucleus are conducted along the myelinized terminals, which when branching, lose their membrane. The authors refer to Katz and Miledi (1965), who showed that in the terminal lamina of the muscles of a frog a change from negative spikes to positive ones is connected with the conduction of impulses through a nonmyelinized terminal branch of the motor axon. Therefore Ito and Yoshida (1966) assume that a similar phenomena may be observed everywhere axons lose their myelin membrane, and in connection with this a change in membrane characteristics occurs. An α wave preserves its negativity, and evidently reflects the impulse current in the myelinized fibers passing through Deiter's nucleus, in particular along its lateral edge. /218

The assumption that α and β waves are generated by two different groups of axons is confirmed, in the opinion of the authors, by the fact that with penetration of axon structure by a microelectrode they reacted to stimulation of the cerebellum with spike potentials during the phase of α or β waves.

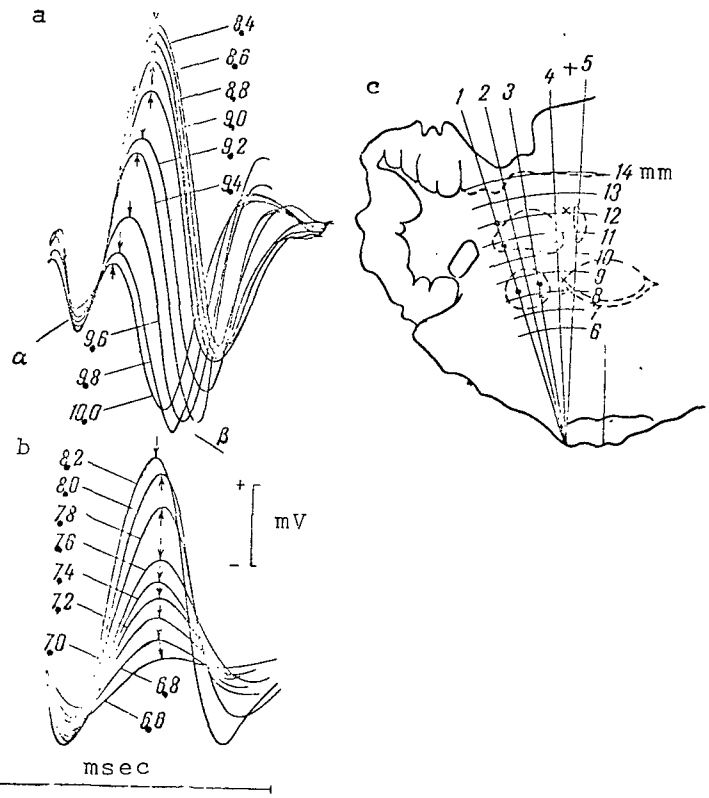

Fig. 66. Origin of α and β Spikes. (a,b) Superposition of Recordings of Focal Potentials Registered With the Conduction of an Electrode Along Tract 2 (cf. Diagram c Where the Depth of Insertion of the Electrode is Indicated) (Ito et al., 1966a).

Thus in the opinion of the authors an α wave is created by impulses conducted with great speed directly from the cortex of the cerebellum to Deiter's nucleus. A β wave is also connected with the propagation of impulses along direct paths but with a slow speed. This is proved by the following facts. /219

In the first place, latency of a β wave depends upon the distance between the point of stimulation and registration. The latency of the wave registered in Deiter's nucleus was 0.36 msec with stimulation of the forward portion of the 4th lobulus, and 0.48 msec with the stimulation of the 5th lobulus (distance between the points: 7 and 10 mm). Thus the speed of conduction is 20 msec. In the second place, β waves elicited with simultaneous stimulation of these lobuli are superimposed upon one another without any interaction, which indicates the absence of convergence with the conduction inside the cerebellum.

The origin of β waves was investigated also by means of stimu-

lation of Deiter's nucleus. In order to avoid stimulation of the paths of α waves, only the dorsal-medial corner of Deiter's nucleus was stimulated, i.e., at the point where only βwaves were registered. If short impulses of current were advanced through the electrode with a duration of 0.2 msec and a force of 20 μA (Wall, 1958; Eccles et al., 1966), it was possible to register negative potentials in the cortex of the cerebellum.

The latency of these potentials was close to the latency of β waves, elicited by stimulation in the reverse direction. If the microelectrode was pulled in the ventral direction along Deiter's nucleus, the effectiveness of the elicited potentials in the cortex of the cerebellum progressively decreased. This dependency was parallel to development of the initial phase of a β wave.

If the hypothesis put forward by the authors were maintained then such a decrease in effectiveness does not appear unexpected, since it is observed with stimulation of the region where endings of the fibers are nonmyelinized.

The authors postulate that negative potentials are elicited in the cortex of the cerebellum through the same nerve paths along which β wave impulses are conducted. Therefore α and β waves are connected with the conduction of impulses along two different paths to Deiter's nucleus with different speeds.

Intervals between the beginning of a β wave and the beginning of early IPSP with stimulation of the 3rd through 5th lobuli on the average equalled 0.51 msec. The duration of 0.51 msec is the value of one synaptic delay for IPSP in the neurons of Deiter's nucleus, i.e., a β wave characterizes the presynaptic flow of impulses eliciting early IPSP.

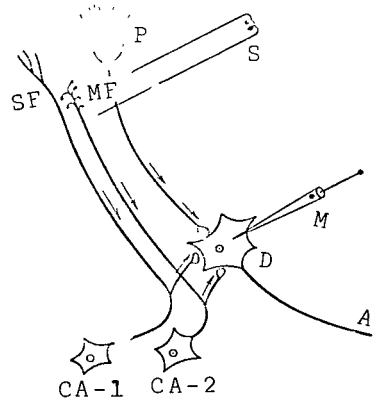

Fig. 67. Schematic Drawing of the Possible Monosynaptic Connections Between the Cortex of the Cerebellum and Neurons of Deiter's Nucleus. P - Purkinje's Cells; D - Neuron of Deiter's Nucleus and its Axon; CA-1 and CA-2-Cells Sending Scansorial (SF) and Mossy Fibers (MF); S-Stimulating Electrode in the Cortex of the Cerebellum; M-Microelectrode. The Arrows Indicate the Direction of Impulses from the Stimulating Electrodes to Deiter's Nucleus (Ito et al., 1966a). /220

It is evident that with the stimulation of the cortex of the cerebellum either directly or indirectly, different neuron structures are excited; not only Purkinje's cells and their axons, but also cerebellar afferents (scansorial and mossy fibers) and cells of the granular layer. Axons of these cells are distributed parallel to the fibers which are connected with Purkinje's cells, basket-shaped cells, Golgi's cells and stelliform cells. Therefore the obtained data present the result of a complex sequence of stimulation of various structures. Actually, as is shown in Figures 64 and 65, stimulation of the cortex (ipsilateral forward portion) elicits various changes in potentials of the neurons of Deiter's nucleus, including IPSP and SPSP and the subsequent excitation after IPSP (Fig. 64).

With intracellular registrations the authors succeeded in precisely defining PSP connected with the conduction of impulses along poly- and monosynaptic paths. Monosynaptic connections from the cortex of the cerebellum to the neurons of Deiter's nucleus may be performed by axons of Purkinje's cell of the ipsilateral anterior portion (Walberg, Jansen, 1961; Eager, 1963) and by the mossy or scansorial afferent fibers which send collaterals of axons to Deiter's nucleus (Fig. 67). According to Lorente de No (1933a) the spinocerebellar fibers also send collaterals of axons to Deiter's nucleus.

Ito and Yoshida (1966) showed that there is a powerful monosynaptic inhibitory path from the cortex of the cerebellum to Deiter's nucleus. This conclusion is especially important from the point of view that the majority of inhibitory neurons has short axons not more than a few millimeters in length. Renshaw's cells (Eccles et al., 1954); Ia inhibitory neurons in the intermediate nucleus of the spinal cord (Eccles et al., 1954); basket-shaped cells in the cortex of the hippocampus (Anderson et al., 1964) and in the cortex of the cerebellum (Eccles et al., 1966). It was noted, /221 however (Eccles et al., 1961a), that monosynaptic inhibition of cells of the ventral spino-cerebellar tract were sometimes deformed by fibers up to 21 mm in length. The data of Ito and Yoshida (1966) showed that inhibitory axons from the cortex of the cerebellum to Deiter's nucleus must be on the order of 10 mm in length.

The inhibitory influences of the cerebellum on the bulbar centers (Pollack, Davis, 1930) are well known. Partial or complete removal of the cerebellum increases discharges of motoneurons elicited by stimulation of the vestibular nerve (Gernandt et al., 1959). Thus the cortex of the cerebellum has tonic inhibitory influences on the underlying centers. Ito and Yoshida (1966) assumed that these inhibitory influences of the cortex of the cerebellum are performed by Purkinje's cells. This point of view was confirmed by the following observations: (1) inhibitory (analysis of extracellular spikes) influences are probably mediated by paths from the cortex of the cerebellum to the neurons of Deiter's nucleus (Fig. 66) through long corticofugal fibers, which pass through the

nuc. fastigii and the nuc. interpositus and enter into synaptic contact with the cells of Deiter's nucleus; (2) with antidromic activation of the inhibitory path, potentials in the cortex of the cerebellum arise which may be considered a consequence of antidromic activation of Purkinje's cells.

This hypothesis is supported by the fact that IPSP arises in neurons of Deiter's nucleus each time that Purkinje's cells are activated through direct or transynaptic paths; monosynaptic and inhibitory influences are localized on the ipsilateral side of the anterior and posterior sections which are in correspondance with the histological borders of the distribution of axons of Purkinje's cells to Deiter's nucleus; only inhibitory influences such as in Deiter's nucleus are registered in all 3 cerebellar nuclei with activation of the cortex of the cerebellum; neurons different from Purkinje's cells which were able to accomplish monosynaptic connections of the cerebellar cortex with Deiter's nucleus have an exciting influence on Deiter's nucleus, which was proved by the stimulation of spinal ascending fibers (Ito, et al., 1964) of primary vestibular fibers (Ito, Yoshida, 1964) and of the olivo-cerebellar fibers (Ito, Yoshida, 1966; Eccles et al., 1966). Neurons of nuc. fastigii also excite neurons of Deiter's nucleus.

Despite the large number of proofs of the inhibitory function of the cerebellum, axons of Purkinje's cells are considered to be exciting. The data of Ito and Yoshida (1966) permit one to consider, with sufficient conviction, that Purkinje's cells have an inhibitory nature and have inhibitory monosynaptic influences on the centers of the spinal cord controlling spinal ascending systems. Monosynaptic SPSP's which were registered in several neurons of Deiter's nucleus (Fig. 65) evidently are connected with collaterals of the /222
cerebellar afferents (CA-1 and CA-2, Fig. 67). The possibility of such an axon reflex is proved by the fact that polysynaptic SPSP's must be connected with axon reflex activation of scansorial or mossy fibers of the neurons, which in turn send exciting impulses to neurons of Deiter's nucleus; inhibition of Purkinje's cells leads to excitation of the neurons of Deiter's nucleus which is comparable with disinhibition of motoneurons (Wilson, Burges, 1962). Such disinhibition, along with axon reflex excitation, could explain the exciting cerebellar influences which were observed by a number of authors (de Vito et al., 1956; Pompeiano et Cotti, 1959).

Axons of Purkinje's cells, including the collaterals are myelinized. Their diameter near nuc. dentatus is 3-6 m (Szentagothai, Schimert, 1941), which corresponds to a speed of impulse conduction of 15-20 m/sec (Hursch, 1939). It is necessary to note that according to Brodal and others (1966) the basket-shaped structures around neurons of Deiter's nucleus are formed by terminals of long corticofugal fibers from the cerebellum. Ito and Yoshida (1966) admit the possibility of considering endings of the axons of the Purkinje's cells on the neurons of Deiter's nucleus as analogous to the endings of the basket cells innervating pyramid cells of the hippocampus

and Purkinje's cells. Such a type of pericellular branching has great significance for the realization of inhibitory influences (Anderson et al., 1964). However axons of Purkinje's cells go not only to the soma and the fixed dendrites of the cells of Deiter's nucleus, but also to the thin dendrites.

Experiments of Szentagothai and Rajkovits (1959) showed that the scansorial fibers leave the inferior olive, and the physiological data of Eccles and coll. (1966) attest to the fact that the olivo-cerebellar path has a powerful monosynaptic exciting influence on Purkinje's cells.

Ito and coll. (1966) assumed that neurons of Deiter's nucleus are inhibited as a consequence of the activation of Purkinje's cells, which served as the object of their investigations.

In experiments on cats under nembutal anaesthesia they studied intracellular potentials in the cerebellum and neurons of Deiter's nucleus with stimulation of various connections of the olivo-cerebellar system.

Purkinje's cells were identified according to the characteristic depolarization potential (Granit, Phillips, 1956) or to the responses along the scansorial fibers (Eccles et al., 1966).

In the investigations of Ito et al., (1966) it was shown that stimulation of the cerebellum elicits the responses of scansorial fibers in Purkinje's cells with a broad spectrum of latency, similar to the spectrum which even IPSP's have in neurons of Deiter's nucleus. Comparatively early responses of scansorial fibers and IPSP may be a consequence of impulsation conducted along scansorial fibers to Purkinje's cells. However latencies of 3-6 msec are too great for the conduction of impulses along intracerebellar paths. The temporal connection of responses in scansorial fibers at IPSP proves the dependency of inhibition in neurons of Deiter's nucleus with stimulation of the olives from activation of Purkinje's cells.

The temporal connection between SPSP of neurons of Deiter's nucleus and responses of scansorial fibers in Purkinje's cells remains strictly constant, despite various points of stimulation in the lower olive and segments of the spinal cord. Also both of these potentials are simultaneously subject to fluctuation of spinal vestibular transmission. Therefore evidently SPSP of the neurons of Deiter's nucleus was elicited from the olive by the same path as responses of scansorial fibers of Purkinje's cells. There are histological data assuming a projection from the inferior olive to Deiter's nucleus (Muskens, 1934; Brodal, 1940). The distance from the superior olive to the contralateral Deiter's nucleus is approximately 10 mm, while the distance from Deiter's nucleus to the deep lamina of the forward portions of the cerebellum is 5 mm. If we assume that the smallest latency (2.4 msec) of SPSP elicited in neurons of Deiter's nucleus with stimulation of the olive was con-

nected with passage of impulses at a distance of 10 mm plus the synaptic delay of 0.3 to 0.5 msec (Eccles, 1966), then it follows that impulses from the olive are conducted at a speed of 5 m/sec, and influences from the olive to neurons of Deiter's nucleus are monosynaptic. The distance in latency between SPSP in neurons of Deiter's nucleus and the response of scansorial fibers equals approximately 1 msec, if we accept that impulses from the olive to the cortex of the cerebellum are also conducted at a speed of 5 msec at a distance of 5 mm, and the time of synaptic delay for SPSP and responses of scansorial fibers is the same. The spectrum of latencies of SPSP can be due to the nature of exciting interconnection in the lower olive.

Thus, direct connections of the labyrinth with the cerebellum and monosynaptic inhibition in neurons of Deiter's nucleus, conditioned by the activation of Purkinje's cells, indicate the close connection of the cerebellum with the vestibular analyzer.

Undoubtedly not only superficial but also deep sections of the cerebellum (which may be assumed on the basis of anatomical data) influence relay links of the vestibular analyzer.

CHAPTER VII

VESTIBULAR INFLUENCES ON THE VEGETATIVE NERVOUS SYSTEM

Connection of the Labyrinth with the Parasympathetic Portion of the Nervous System

Influences from the vestibular apparatus possibly may be considered to dominate in the development of "motion sickness". Bard and others (1947) showed that the nodulus and uvula of the cerebellum are also connected with the development of "motion sickness". Borison and Wang (1949, 1950) conducted an extensive analysis of the mechanism of vomiting. /224

Numerous data testify to a whole series of vegetative disorders connected with "motion sickness", (cf. the survey of Spiegel, 1946; Khechinasvili, 1958). There is no doubt that such symptoms as drowsiness, growing pale in the face, cold sweat, increase in saliva production, nausea and vomiting are connected with coordinated activity of the vegetative and somatic systems. Evidently the afferent vestibular impulses reach centers in the periphery of the vegetative nervous system. However the paths of such impulses are not studied. Carpenter (1960) assumes the existence of fibers from the vestibular nuclei to nuc. solitarius, and hence to the dorsal motor nucleus nuc. vagus.

The literary data (Tyler, Bard, 1949; Khilov, 1950; Shiraiwa et al., 1963, and others) allow us to assume a certain instability of the central control of the vegetative nervous system which makes some persons more sensitive to motion sickness than others. Hypo- and hyper-reflex conditions are defined by the sum of exciting and vestibular influences converging on the terminal general paths, either of the vegetative or somatic motor output. Gernandt and Gilman (1959, 1960) described tonic inhibitory influences from the higher centers on the vestibular nuclei (cf. Chapter V). Are there similar influences on the vegetative nervous system?

Undoubtedly the study of tonic and phase control over the vegetative nervous system, as well as study of the effectiveness and physiological characteristics of the central processes, connected with the conduction and distribution of impulses from the vestibular apparatus to the centers of the vegetative nervous system and its efferent fibers, permit us to reveal the mechanisms of motion sickness.

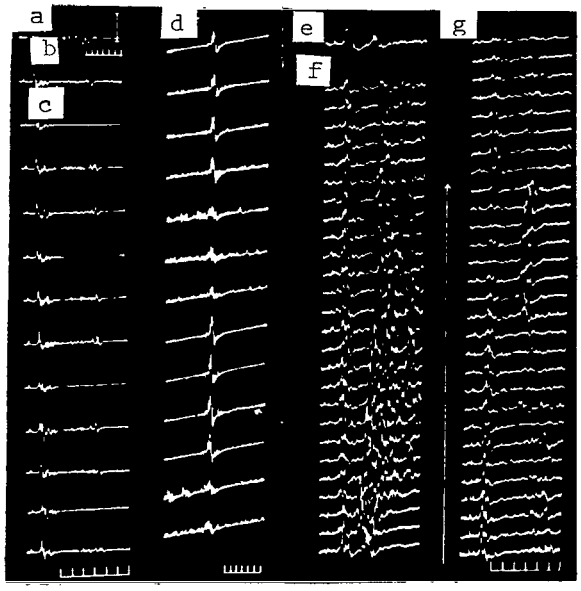

Fig. 68. Responses in the Ipsilateral Vagus Nerve to Stimulation of the Vestibular Nerve. /225
(a, b) Responses to Single Stimulation with Various Scanning Speeds; (c, d) Interaction of Responses of the Vagus Nerve to Stimulation of the Vestibular Nerve at a Frequency of 1 Hz (c) and 3 Hz (d) with Rhythmic Background Activity, Elicited by the Respiratory Center; (e) Responses to Frequency of Stimulation of 1 Hz; (f) 10 Hz; (g) Continuation (Indicated by the Arrow) of column f. Time Scale: 1 msec (a); 5 msec (b, c, e, f, g); 10 msec (d) (Akert, Gernandt, 1962).

The Vestibulo-vagal response reactions were studied in experiments on cats by Akert and Gernandt (1962).

Stimulation of the vestibular nerve by a single stimuli elicited responses in the central end of the ipsilateral n. vagus. In the contralateral n. vagus responses were not detected.

Latency of response is equal to 4-5 msec: amplitude to 0.1 - 0.2 m V. The second, smallest response, removed from the initial one by 20 msec, had a higher threshold than the first and depended upon the background activity registered in the central end of the vagus nerve (Fig. 68). /226

With registration from the central end of n. vagus, small spindle-shaped discharges with a frequency of 15-20/min. and a duration of around 2.5 msec could be observed. These discharges were elicited by impulsation from the respiratory center to the nucleus of n. vagus. They were registered even after temporary cessation of artificial breathing in a curarized animal.

Another type of rhythmic activity in efferent fibers of n. vagus depends upon vago-vagal impulses (the Herring-Brayer reflex) originating from the receptors of the lungs. These discharges are clearly connected with respiratory movements of the thorax with inhalation: bursts of impulses, during exhalation the discharges are absent. This type of rhythmic activity disappears with interruption of artificial breathing. It is conditioned by activation of the peripheral receptors and by afferent impulses conducted

along an intact n. vagus and through vago-vagal connections. With registration from the whole nerve such activity is masked, but by activity generated by the respiratory center; therefore registration from separate fibers is necessary in order to discover it.

Responses in n. vagus to single stimulation of the vestibular nerve depended upon temporal correlation between the beginning of stimulation and the appearance of the spindle activity elicited by the respiratory center (Fig. 75). If the response came during the time interval between the two spindles, the amplitude of the initial response was large and a delayed response of lesser amplitude was observed. If the response to stimulation of the vestibular nerve was superimposed on the spindle activity, then the initial response was strongly suppressed and a second response was not noted. In the cases when the frequency of stimulation of the vestibular nerve does not correspond to the frequency of spindle sequence, the response was strengthened or weakened depending on whether it was in phase with rhythmic bursts of the spindles or not.

Thus in the competition for entry to the nucleus of n. vagus between impulses from the respiratory center and impulses elicited by vestibular stimulation, the first dominate. But as was shown with the study of the registrations from separate fibers of n. vagus, vestibular impulses also influence the respiratory spindles. This effect is especially pronounced with a frequency of stimulation of the vestibular nerve of 10 imp/sec; the frequency of rhythmic spindle activity increases, and irregular discharges of great amplitude can appear.

Amplitudes of responses in n. vagus to stimulation of the vestibular nerve were more variable than amplitudes of segment signal reflexes or amplitudes of responses in the ventral roots (Gernandt et al., 1957; Gernandt, Gilman, 1960).

Despite the great variations of amplitudes of responses in n. vagus to vestibular stimulation, it was still possible to establish that the primary responses do not change their amplitude significantly with an increased frequency of stimulation. Thus with an increase in frequency of stimulation to 5 imp/sec, it was possible to observe a weak increase in the amplitude of primary responses; an additional increase in frequency led to a slight decrease in the amplitude of responses. /227

On the other hand, the secondary delayed response depended upon the frequency of stimulation. With a frequency of stimulation of the vestibular nerve of 10 imp/sec, the latency of responses increased. With continued stimulation responses became smaller and finally disappeared entirely (Fig. 68). Vagal responses to vestibular stimulation were strongly increased if decerebration were performed on the cat under chloralose anaesthesia. The secondary response disappeared after this type of sectioning. This effect lasted for 1 hour.

The character of responses to stimulation of the vestibular nerve with registration from single fibers of n. vagus was the same as with removal from the entire nerve.

Vestibular activity has a stronger influence on afferent vagal reflector discharges in n. vagus than on discharges generated in the nucleus of n. vagus by the respiratory center. With a single stimulation of the central end of the sectioned contralateral n. vagus, one response for a latency of 5 msec and duration of 10 msec was registered in the ipsilateral n. vagus. If a single stimulation of the vestibular nerve preceded this response, the vagal response was absent for 100 msec. Thus with stimulation by single impulses the vestibular influences suppressed the vago-vagal reflex. If the contralateral n. vagus was stimulated earlier, then its influence on responses to stimulation of the vestibular nerve could not be detected.

Similar interaction was traced even with the intact contralateral n. vagus when physiological activation of peripheral receptors led to the vago-vagal discharge. The dominating vestibular influences were seen very clearly in this case. If the vestibular influences somewhat precede activity on inhalation, then the vago-vagal discharge is retarded. If the stimulation of the vestibular nerve corresponds in time with the vago-vagal reflector discharge, then the latter is interrupted by 100 msec. With a frequency of vestibular nerve stimulation of 10 imp/sec, the vago-vagal discharges are suppressed throughout the period of stimulation.

The latency of responses in n. vagus with stimulation by separate stimuli was 4-5 msec; in n. phrenicus around 15 msec (Gernandt, 1964). The effect of n. vagus is ipsilateral; in n. phrenicus, bilateral. The threshold value of response reaction for n. phrenicus is 3 times higher than for n. vagus. Thus, thresholds with activation of the vegetative nervous system are lower than for the somatic system.

As was noted above, with a high frequency of stimulation of the vestibular nerve (10 imp/sec) the amplitude of responses in n. vagus did not essentially change or even slightly decrease. /228
On the other hand, in n. phrenicus the amplitude of responses increased and the latency decreased. With continuous stimulation of the vestibular nerve over several minutes the character of responses remained as before. The amplitude of responses in n. phrenicus was significantly higher than in the control and after cessation of stimulation gradually returned to the original value. These experiments clearly demonstrate the difference in the effect of temporal stimulation between the efferent fibers of the vegetative and the somatic systems during vestibular stimulation.

Exactly the same differences were observed even with simultaneous registration in n. vagus and the ventral roots at the level L_7. In order to determine whether tonic inhibitory impulses influence the nuclei complex of n. vagus and counteract temporal summation, decerebration was performed on the intercolicular level. It was discovered that decerebration strengthened responses in n. vagus to stimulation of the vestibular nerve and also facilitated responses in the vestibular roots. New thresholds of vestibulo-vagal responses were as formerly lower than thresholds of vestibulo-spinal responses, but the differences were insignificant.

With the application of paired stimuli in decerebrated cats the amplitude of vestibulo-vagal responses to a second stimulus was less than to the first, while in the ventral roots the amplitude of responses to the second stimulus was increased. Insofar as vagal responses, as well as responses in the ventral roots, were of increased amplitude after decerebration, this effect may be attributed to removal of the inhibitory tonic influence of the higher sections of the central nervous system to the vestibular nuclei and the adjacent reticular formation. Decerebration did not influence the vago-vagal response reactions, and as before there was no temporal summation. Thus facilitating vestibulo-vagal responses after decerebration was conditioned by selective liberation of vestibular nuclei from tonic inhibitory influences, which permits a more powerful flow of impulses to reach the nuclei of n. vagus.

Neither the destruction of the anterior portion of the cerebellum nor full cerebelectomy in combination with postbrachial section of the spinal cord could lead to a strengthening of the vago-vagal reflex. At the same time these structures have powerful inhibitory influences on the vestibular nuclei (cf. Chap. 6).

Detailed data on the influences of stimulation of the vestibular nerves on the respiratory center were obtained with simultaneous registration of activity in the central end of n. vagus and n. phrenicus. Rhythmic activity connected with inspiration began to be registered in n. vagus and in n. phrenicus. After the original discharge in n. vagus, a secondary discharge with a short interval followed. The vestibulo-vagal responses were decreased if they were superimposed on any of the phases of the respiratory cycle.

A few seconds after the beginning of stimulation of the /229
vestibular nerve with a frequency of 10 Hz, changes in respiration appeared. The initial spindle activity of n. vagus and n. phrenicus corresponding to the phases of the respiratory cycle decreased in

amplitude and duration. Stimulation of the vestibular nerve shortened the phase of inspiration and accelerated respiration but could not change the regularity of respiratory discharges. The respiration rate increased from 16 to 20/min. In addition the connection between discharges of inspiration and expiration in n. vagus were never disturbed, but irregular high amplitude spindle-shaped discharges could appear. They could be observed in any phase of the respiratory cycle. If they were observed in the inspiration phase, then at this moment impulsation in n. phrenicus was completely suppressed.

In control experiments with stimulation of the contralateral n. vagus, respiratory neurons were discharged uninterruptedly, judging by the activity of the ipsilateral n. vagus. With a 10 Hz stimulation, irregular bursts of high amplitude, short duration impulses appeared, where upon the low amplitude activity of n. phrenicus when such bursts appeared. After cessation of stimulation the impulsation of low amplitude in n. vagus was prolonged a few seconds; in addition, the activity in n. phrenicus completely stopped. Gradually the spindles of rhythmic activity appeared again, and in one minute spontaneous activity reached the original values.

Insofar as simultaneous stimulation of the vestibular nerve and the contralateral n. vagus leads to an increase of vagal output of impulses from the respiratory center, this impulsation interacts with the vestibulo-vagal or vago-vagal reflex discharges. In order to investigate whether this interaction is the cause of the absence of temporal summation of parasympathetic reflector responses, Gernandt (1964) introduced nembutal intravenously in an amount which suppressed rhythmic bursts of discharges which were connected with respiration, in n. vagus, but did not change the nature of the vestibulo-vagal reflex responses and the vago-vagal reflex responses. With an increase in the frequency of stimulation of the vestibular nerve, a decrease in amplitude of vestibulo-vagal responses was observed. The vago-vagal responses were also significantly decreased in amplitude and sometimes did not appear at all. Thus, despite the absence of influences from the respiratory center, responses in the vegetative nervous system were decreased in amplitude and a temporal summation was absent. After the introduction of nembutal, temporal summation in the ventral roots did not undergo changes.

Stimulation of almost any sensory nerve changed respiration which could be reflected in the impulsation in n. vagus. It was established that stimulation of dorsal roots, synchronized with /230
stimulation of the vestibular nerve or somewhat mixed at a frequency of 1 imp/sec, had either weak influences on the vestibulo-vagal responses or did not show them at all. However, with stim-

ulation of the dorsal roots or of n. splanchnicus at a frequency of 20-30 imp/sec, the vestibulo-vagal responses were suppressed. With stimulation of the vestibular nerve at the same frequency, vagal response reactions of n. splanchnicus were suppressed.

Before impulses from the labyrinth reach the nuclei complex of n. vagus they pass through the vestibular nuclei and the bulbar reticular formation.

Any change in tonic or phase influences on this intermediate relay changes the activity in the outburst of the vegetative and somatic systems. These data and also those considered in Chapters 5 and 6 demonstrate the existence of a powerful tonic inhibitory control of vestibular reflexes. But these tonic influences do not prove to be propagated to the vagal nuclei. Lacking anatomical data on the vestibulo-vagal connections, it may only be assumed that they exist through the cells of n. solitarius. The cells of the dorsal motor nucleus of n. vagus are comparatively small with a small number of dendrites, but they are longer than the dendrites of the motor cells of the spinal cord. It is possible that this to some degree explains the difference in their functional behavior in relation to temporal summation. It is possible to expect that a neuropile formed by the bodies of the dendrites, is activated with vestibular stimulation, and that the tree-shaped branching of a few dendrites of the vagal cells cannot establish a sufficient connection for the conduction of vestibulo-vagal impulses, in comparison with that /231 which exists in the neuron organization for transmission of vestibular influences to the motor cells of the spinal cord (Eccles, 1959; Rall, 1959, 1960).

The effect of temporal summation on effector organs of the vegetative nervous system evidently may be explained by the liberation of actocholine or substances similar to acetocholine in the nerve endings. Vagal responses were clearly pronounced with stimulation of the vestibular nerve at a frequency of 1 imp/sec and were not seen at a frequency of 20 imp/sec. On preparations of an isolated heart, the inhibitory effect was observed with a frequency of stimulation of n. vagus from 10-100 imp/sec (Joung, Upham, 1961). If stimulation were conducted over a long interval of time then the heart reacted only to the low frequency of stimulation. Insofar as with stimulation of the vestibular nerve at a frequency of 10 msec a response in n. vagus was always registered, there is every basis to expect a cumulative humoral effect on the vegetative effector organs.

The differences in thresholds to vestibular stimulation for motor output of vegetative and somatic systems possibly explain why, with motion sickness, visceral symptoms first predominate

and later somatic effects in the form of vomiting appear. The appearance of kinetic reflexes with an intensive stimulation of the labyrinth is important for the maintenance of vertical posture. If the threshold for the somatic system with stimulation of the labyrinth were lower than for the vegetative, then complex compensatory motor activity would be aimed at diminishing or removing the effects of various forms of vestibular stimulation upon the vegetative effectors. On the other hand, the presence of a number of tonic inhibitory influences on the vestibular system may remove involuntary muscular contractions in response to weak stimulation of the labyrinth, which in the opposite case might interact with coordinated voluntary muscular activity. However at the present time it is still difficult to explain why stimulation of the labyrinth leads to the development of such a non-integrated and destructive syndrome as "motion sickness" which does not have any evident protective function.

Neurons of the respiratory center are excited by nerve impulses transmitted through collaterals of a majority of ascending afferent tracts and from cranial cerebral nerves. It is possible to assume that autonomic change in respiratory rhythm of the medullar centers is maintained by impulses from the pneumotaxic center and the nucleus of n. vagus influencing respiratory centers, which in turn rhythmically inhibit the activity of the inspiration center (cf. surveys of Liliestrand, 1958). The increase in impulsation from the vestibular nuclei shortens discharges in n. vagus upon inhalation and increases the rate of respiration. The increase in respiration rate may also be related to a shortening of the exhalation phase.

Stimulation of the vestibular nerve increases the rate of respiration but simultaneously the vestibulo-vagal response reactions are suppressed which inhibits entrance of vestibulo-vagal impulses to the vegetative effectors. However, this phase respiratory control is insufficient to hinder development of sea sickness. At this time the well-known benefits of deep breathing on shortening the duration of nausea may be explained by the data.

The extensive somato-visceral effects observed in response to vestibular stimulation lead to subsequent activation of various receptor systems (proprioceptors of muscles, vessels, tendons, of Pacini's corpuscles, etc.). The flow of impulses proceeding from them may have phase influences and modulate the parasympathetic motor output in response to vestibular stimulation.

The Significance of the Limbic System in the Activation of the Parasympathetic Nervous System with Stimulation of the Labyrinth /232

The posterior cingulate cortex, the fornix and the dorsal hippocampus were simulated by means of coaxial bipolar electrodes (Akert, Gernandt, 1962). Registration was carried out in n. vagus

and the ventral hippocampus. With stimulation of the cingulate cortex, the response consisted of two spindle-shaped impulse discharges. The latent period of the first was 9-13 msec with a duration of 20 msec; the second had a latency of 40-50 msec, duration 10 msec. Responses with stimulation of the fornix have approximately the same characteristics but differ in the nature of temporal passage. The primary and secondary responses appeared, respectively, in 8 and 35 msec. Stimulation of the dorsal hippocampus elicited responses in n. vagus which were similar to responses with activation of the fornix; after the first series of impulse discharges a delayed series followed with a latency of 10 msec. As in the case of various responses elicited with stimulation of the cortex cingulate and the fornix, the primary responses in n. vagus with stimulation of the hippocampus are connected with the activation registered in the ventral hippocampus; secondary responses did not have an obvious reflection in the activity of the ventral hippocampus.

Responses in n. vagus with rhythmic stimulation of the limbic system manifest a very limited capacity for temporal summation. With an increase in frequency of stimulation from 1 - 3 msec responses in n. vagus are registered, and with a higher frequency, visible response in the whole nerve disappears. These data are strengthened also by the fact that there are no discharges in n. vagus with swift synchronic rhythms in the hippocampus. Only slow theta-rhythms of the hippocampus are reflected in discharges in n. vagus.

Responses in n. vagus elicited by stimulation of the investigated sections of the limbic system depended upon the activity of the respiratory center. They were strengthened and weakened synchronically with the activity of the center, becoming greater between rhythmic discharges from the respiratory center and smaller during these discharges. The respiratory discharges registered in n. vagus are not reflected in the activity of the ventral hippocampus.

Stimulation of the hippocampus during 5 sec. at a frequency of 100 msec was expressed by the appearance in n. vagus of from 3 - 5 synchronic spindles of great amplitude. When the amplitudes of hippocampal discharges reached a maximum, activity in n. vagus completely disappeared, despite the fact that hippocampal discharges activate various anatomical, physiological systems (Fig. 69.) This fact agrees with the observation of Kaada and Jasper (1952) who noted cessation of breathing with stimulation of the rostral hippocampus in man.

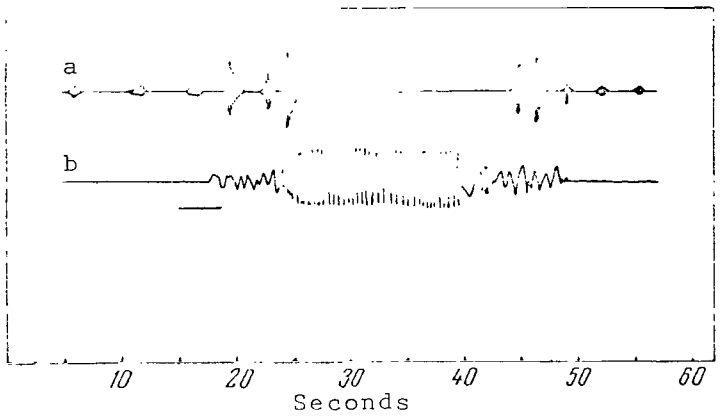

Fig. 69. Influence of the Hippocampus on n. vagus. (a) Left n. vagus; (b) Left Hippocampus (Akert, Gernandt, 1962). /233

During the last "clinical" stage of disturbances in the hippocampus, a short series of prolonged discharges again appeared in n. vagus, and then activity connected with impulsation from the respiratory center was restored, This effect was observed constantly with repeated actions.

If responses in n. vagus to stimulation of the limbic system preceded the vago-vagal reflex discharge elicited by natural activation of the peripheral receptors and conducted centrally through the intact vagus nerve, the reflex discharge was suppressed by 100 msec. Stimulation of the hippocampus with a frequency of 3 msec completely suppressed the Herring-Brayer reflex. However with high frequency stimulation a reflex blockage weakens. This fact assumes the existance of a connection between the limbic system and the nuclei of n. vagus. It is assumed that of all structures, the rhinencephalon and hippocampus present the highest level of integration (Green, 1960). However stimulation of the vestibular nerve by single stimuli did not yield a primary elicited response in the ipsilateral ventral hippocampus, but caused the appearance of spindles with a delayed theta-rhythm. These waves in the ventral hippocampus were discovered even with stimulation of other afferents (Green, Arduini, 1954, and others). With high frequency stimulation of the vestibular nerve neither primarily elicited responses nor any other change in activity in the ventral hippocampus were registered. These data attest the absence of interaction of the labyrinth with the hippocampus.

Stimulation of the vestibular nerve suppresses responses from all investigated sections of the limbic systems in n. vagus for 200 msec. Preceding activations of the cingulate cortex, the /234

fornix or the hippocampus has an insignificant influence on the primary vestibular response; secondary response is suppressed for a period of more than 100 msec.

Thus, according to their significance in directing the vagal efferent discharge, various central structures and peripheral sources are distributed in the following sequences: the respiratory center, the labyrinth, the limbic system, the afferents of n. vagus, afferents of the trigeminal nerve (Akert, Gernandt, 1962).

It was established that stimulation of the limbic system may elicit various visceral reactions (Kaada, 1951; van Buren, 1958). MacLean (1949) proposed calling the limbic system the "visceral brain". Large amplitudes of responses in n. vagus with stimulation of the limbic system permit us to propose that efferent fibers of n. vagus are activated by limbic structures. Early discharge in n. vagus with stimulation of the dorsal hippocampus is registered at the neck level after 9 msec. This latency is comparable with latency for conduction of impulses from neurons of the motor cortex to the spinal cord. Besides the primary discharge in n. vagus, discharges of the second and third order are registered. They allow us to assume a more complicated change. It is possible even for visceral motor innervation that a system exists which is analogous to the extrapyramidal system.

Limbic and vestibular influences converge on the nucleus of n. vagus either directly or through the reticular formation. Akert and Gernandt (1962) propose interpreting the fact that the limbic influences on the nucleus of n. vagus are blocked by preceding stimulation of the vestibular nerve as the appearance of occlusion.

Even another level of interaction of the systems is evidently possible. This is proved by the fact that the hippocampus activity elicits blocking of only the fast response in n. vagus with vestibular stimulation. Insofar as these last responses disappear after decerebration at the intercollicular level, the places of such interaction may be the telencephalon and the diencephalon. The possibility of integration of vegetative reactions with activation of the labyrinth at this level is also proposed by Berney (1960). With rotation of rabbits he observed a drop in arterial pressure (often after rotation). After removal of the cortex it could even be increased. Section at the intracollicular level lowered the arterial pressure and the pulse rate. We obtained similar data (cf. Chap. 9).

The possibility was not excluded that the vestibular projection zone in the flocculo-nodular portion was connected with extrahippocampal structures. Thus Anand and coll. (Anand et al., 1959) showed that stimulation by single stimuli of the flocculo nodular portion may elicit responses in the cingulate cortex, amigdal, and hippocampus. /235

Finally, there may be interaction at the level of the cortical projections of the vestibular apparatus and n. vagus (Chenigovski, 1967).

Change of Impulse Activity of the Respiratory Neurons with Action of Alternate Linear Accelerations

Experiments were conducted on adult cats of both sexes weighing from 2.5 to 3 kg with chloralose nembutal anaesthesia (chloralose 40 mg/kg + nembutal 5 mg/kg intra-abdominally)[9]. The cats' heads were fixed on a stereotaxic instrument, sinciput upwards.

Entrance to the investigated regions of the medulla oblongata bone. The occipital bone was liberated from the muscle by the dull method, after which an opening 1 cm in diameter along the central line near the atlanto-occipital articulation was bored with an electric drill. Next the dura matter was opened and the surface of the brain was dried of cerebrospinal fluid with a hemostatic sponge.

Pulsation of the brain was decreased by lining its exposed surface with a solution of agar-agar at a temperature of 37°.

Impulse activity of the respiratory neurons of the lateral region of the medula oblongata was removed extracellularly with glass microelectrodes with an external tip diameter of 1-3 μ and a resistance of 15-35 Mohm, filled with 2.8 M solution of KCl.

Impulsation of the neurons was recorded on a magnetic tape (magnetophone MAG-8) through an UPT1-01 amplifier with subsequent registration on a KN-4 movie film from the screen of a two-ray oscilloscope EMOF2-01 or "Sanei". With the aim of identifying respiratory neurons, they registered biopotentials of diaphragm muscles, amplification of which was made with the aid of the UVP1-02 amplifier. Access to the diaphram muscles was through the abdominal cavity. An active electrode, made from a small fish-hook, was applied to the diaphragm muscle and a passive electrode was placed on the skin of the animal.

Synchronic registration of impulse activity of neurons and activity of diaphragm muscle permitted the respiratory neurons to be visually separated. Those neurons which gave vollies of impulses synchronic with phases of respiration were considered to be respiratory. Inspiratory neurons displayed volleys of impulses synchronically with an increase in activity of the diaphragm muscle, expiratory neurons displayed volleys of impulses during the diaphram's rest period. Inspiratory neurons with constant /236

[9] Experiments performed by L. A. Rakavitch.

impulse activity increased in frequency of impulsation during inhalation; expiratory neurons increased frequency of impulsation during exhalation.

Stimulation of the otolith portion of the vestibular apparatus was made by rocking the animal in a vertical plane on a special stand (cf. Chapter 3) with an acceleration of 0.8 - 1.2 g. The maximum sweep of oscillations along the vertical was 45-50 cm; the frequency of rockings 45-50/min; the period of 1 oscillation equal to 1.2 - 1.4 sec; duration of rocking 20-60 sec.

Of the 106 inspiratory neurons registered, 62 neurons displayed clear volley impulse activity, synchronized with the activity of the diaphragm muscle. Usually the frequency of impulses in a volley gradually increased, attaining a maximum after which it either very swiftly decreased or impulsation stopped.

Of 54 registered expiratory neurons, 23 were characterized by volley activity in the rest phase of the diaphragm muscle. In several neurons the impulse frequency was constant throughout the volley; in others the impulse frequency attained a maximum in the middle of the volley and then smoothly decreased. It is necessary to note that the impulse frequency in the volley both of inspiratory and expiratory neurons and also the number of impulses broadly varied in different neurons. However, each actual neuron was characterized by a constant volley configuration and the number of impulses per volley.

The remaining neurons (44 inspiratory and 31 expiratory) were characterized by constant activity, the frequency of rhythmicity of which increased during the phase of inhalation or exhalation. Strict constancy of impulse frequency at various times of registration was not characteristic for neurons with constant activity.

With rocking in the vertical plane the respiration of the animal, as a rule, was curtailed. This curtailment took place due to prolongation of the exhalation phase in comparison to inhalation. Sometimes a linking of the rhythm of rocking with that of breathing was observed. Linked rhythm in some cases was maintained for 1-15 sec after the cessation of rocking.

Volleys of inspiratory neurons, as a rule, were shortened; the number of impulses per volley was reduced and interspike intervals were decreased (cf. Fig. 70). With several neurons, linking of rhythm was discovered, which is visibly demonstrated on the correlation functions of interimpulse intervals (Fig. 71, cf. Chap. 9, Section 3). It was often possible to see that the rhythm of rocking was bound to a neuron, while respiration was cut off. In addition, during the 30th-40th second of rocking, the neuron began to generate constant rhythmicity; it reacted to motion of the platform both up and down and sometimes reacted to motion in only one direction.

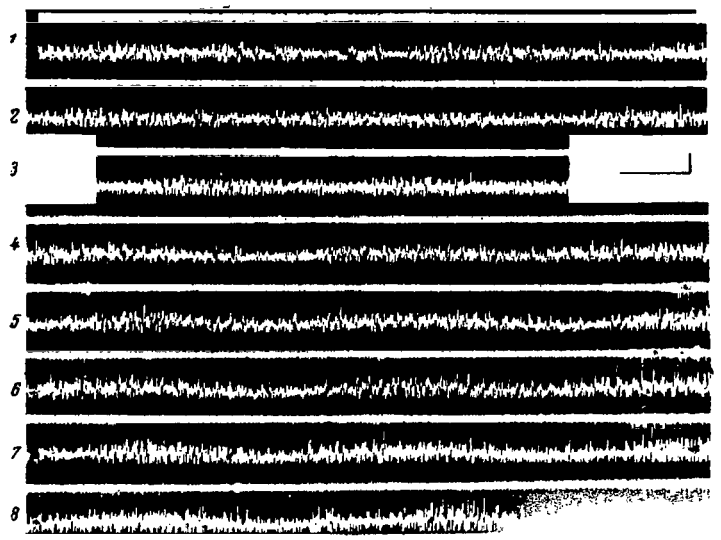

Fig. 70. Impulse Activity of the Inspiratory Neuron with Rocking /237
on Each Recording the Upper Ray Indicates Impulse Activity of the Neuron, the Lower Ray Indicates Activity of the Diaphragm Nerve. (1, 2, 3) Background. (4-8) Rocking. Time Scale: 0.25 sec. Calibration: 250 μV (According to Radkevich).

With the aid of the autocorrelation analysis method (cf. Chap. 9), the change in interspike interval in correspondence with the rhythm of rocking was made apparent.

In the majority of discharge expiratory neurons, prolongation of the volley was observed; i.e., impulses appeared during the rest period. Often the density of the neuron became almost constant. By the method of correlation analysis it was possible to show a change in interspike interval in the volley when it was prolonged for more than one period of rocking, in the rhythm of rocking (Fig. 72). If rhythmicity of the neuron became constant, then also the rhythm of rocking was seen in its impulse activity.

Impulse activity of constant expiratory and inspiratory neurons in the majority of cases increased in frequency with rocking but even curtailment of rhythmicity was observed. Several neurons with continuous activity began to generate discharge activity, whereupon discharges were manifested in the rhythm of rocking (Fig. 73). Other neurons, characterized by constant rhythmicity with an increased frequency of impulse activity in corresponding phases of respiration, revealed the appearance of changes in interspike intervals in the rhythm of rocking. In several cases these changes were

observed only on one direction of the motion of the platform; other neurons reacted to both directions of motion.

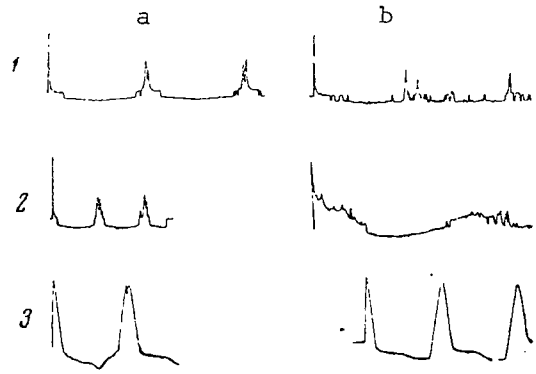

Fig. 71. Correlation Functions of Interspike Intervals of Inspiratory Neurons. (a) Background; (b) Rocking; (1-2) Various Neurons; (3) After Bilateral Labyrinthectomy (According to Radkevich). /238

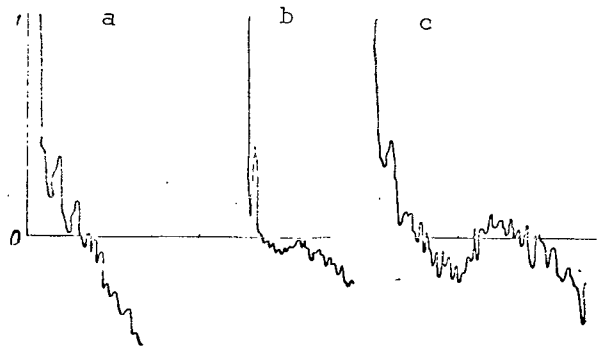

Fig. 72. Correlation of the Functions of Interspike Intervals of One Discharge of the Expiratory Neurons. (a) Background Activity; (b, c) 10th and 30th Second of Rocking (According to Radkevich).

Three expiratory neurons were registered, the impulse activity of which increased at the moment the rocking began, and after 10-15 seconds they became completely silent and restored activity only after 3 minutes after cessation of rocking.

Thus under conditions of adequate stimulation of the otolith portion of the vestibular apparatus in cats by vertical rockings, characteristic changes in respiration were established. They were

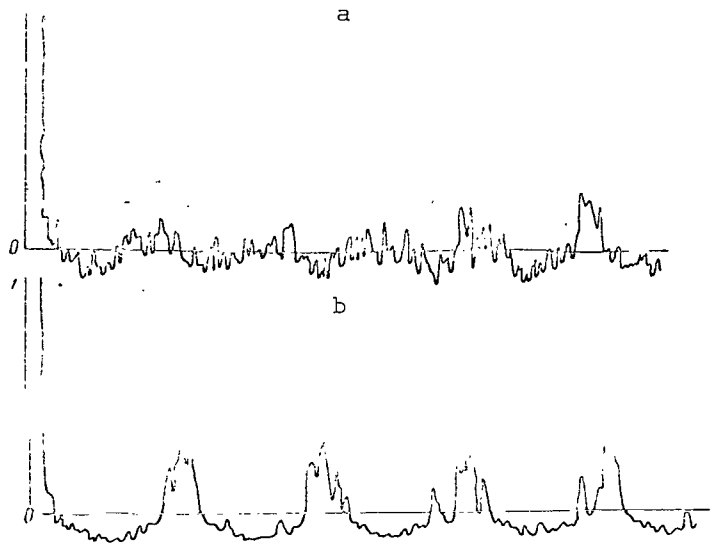

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Fig. 73. Correlation Functions of Interspike Intervals of the Respiratory Neurons. (a) Background Activity (Constant); (b) Activity of the Same Neurons with Rocking (Bundled) (According to Radkevich).

expressed in some cases by the cutting of breathing with a change in the structure of the respiratory cycle in the form of prolongation of the exhalation phase, in comparison with the background value, and shortening of the inspiration phase. In other cases a linking of the rhythm of stimulation to that of respiration took place. Impulse activity of the respiratory neurons of the lateral regions of the medulla oblongata also changed. In the majority of neurons an increase in impulse activity and a shortening of the interspike interval were noted. Latency of volley of inspiratory neurons, as a rule, was shortened, and a volley of expiratory neurons was lengthened. Sometimes these and other neurons began to generate constant rhythmicity, but most frequently this was observed in expiratory neurons. The method of correlation analysis succeeded in showing the change in interspike interval in all neurons with the rhythm of rocking in the case when evident linking of rhythm was not visually observed. Linking of rocking rhythm to neurons took place even when the same respiratory movements did not acquire the rocking rhythm and were even somewhat curtailed. It is necessary to note that in some cases reactions of respiratory neurons began exactly at the beginning of rocking and others only after 5-20 seconds. Sometimes reaction began only after cessation of /240 rocking. In neurons with a sharp reaction at the end of rocking

(60th second), almost complete restoration of impulse activity to background values was observed.

A shift of discharge in relation to the corresponding phase of respiration which is especially visibly manifested on inspiratory neurons could be observed on discharge respiratory neurons with rocking. Under conditions of rocking, discharge was manifested earlier than spindle activity of the diaphragm muscles by 0.1 - 0.04 sec.

In the control group of animals with a bilateral labryinthectomy a significant cutting of respiration due to prolongation of the exhalation and inhalation phases was noted. In comparison with intact animals, the incidence of expiratory discharge neurons was increased in comparison with discharge inspiratory neurons. The duration of discharges increased. The incidence of respiratory neurons with constant activity is significantly lessened whereupon the impulse frequency is decreased.

Under conditions of vertical rocking the frequency of respiration was not changed, and even the impulse activity of the majority of registered neurons (Fig. 71) was not changed. However, it follows to note that in 5 of 57 registered neurons, cutting of impulse activity was discovered. Neither visually nor with the aid of the autocorrelation method could a periodic change in the interspike interval with rhythms of rocking be observed in these respiratory neurons with constant activity. Such neuron behaviour is probably connected with extralabyrinth influences which cannot be completely excluded in experiments.

The Role of the Functional Condition of the Respiratory Center on the Reactions of Respiratory Neurons to the Action of Alternate Linear Accelerations

With the goal of lowering excitability of the respiratory center, a bilateral section of vagal neurons was made. In order to do this, a longitudinal cut in the skin on the neck of the cats was made after preliminary anaesthetization of this region by 0.5% novocaine and the vascular nerve bundle of the internal carotid artery was separated out. Then the vagus nerve was prepared and severed. Vagotomy elicited a significant curtailment of breathing.

As in animals with preserved vagus nerves rocking produced a curtailment in the breathing rate but not once was linking of the rhythm of rocking observed. As in the preceding series of investigations, discharges of inspiratory neurons were lengthened; discharges of expiratory neurons were shortened. However in vagotomized animals the reaction of respiratory neurons in the form of complete inhibition of impulse activity was more pronounced. Autocorrelation analysis of interspike intervals showed the presence of periodicity with the rhythm of rocking.

In another series of experiments a change in excitability /241
of the respiratory center was attained by blocking the reticular formation with etaperazine. Etaperazine elicited significant lowering in respiration rate; respiration became infrequent and deep. The impression was received that the incidence of respiratory neurons was essentially lowered. Not one expiratory neuron with constant impulse activity could be registered; the incidence of inspiratory neurons with constant rhythmicity was lessened. Thus 14 discharge and 12 constant activity inspiratory neurons and 13 expiratory neurons with discharge activity were registered.

With rocking, the respiration was cut down to 1-3 respiratory movements per minute. Linking the rhythm of rocking to that of respiration was not observed. The frequency of impulse activity in the majority of neurons was lowered. Expiratory discharges were extended, inspiratory discharges were shortened in some neurons and extended in others. Sometimes neurons with volley activity began to generate constant rhythmicity; in addition, respiration insignificantly decreased. Sensitivity of respiratory neurons to change in the value of acceleration expressed in a periodic change in the interspike interval in the rhythm of rocking was preserved.

The effect of elevation of excitability of the respiratory center was achieved by means of subcutaneous introduction of 1 ml of an ampoule solution of lobeline. In addition, a short-term (1-2 min) increase in the respiration rate was observed, as well as an increase in the amplitude of diaphragm activity. The number of impulses in volleys of inspiratory neurons increased; volleys of expiratory neurons were prolonged.

On the background of the introduction of lobeline, the stimulation of the labyrinth elicited minimum reactions of respiratory neurons, in comparison with reactions in intact and vagotomized animals. The phenomenon of linking of rhythm of vestibular stimulus to respiration was not observed. The impulse frequency in all groups of neurons remained practically unchanged. Discharge respiratory neurons preserve the character of their activity in correspondence with the phases of the respiratory cycle. However, the reaction was preserved in the form of a periodic change in interspike intervals of discharge in the rhythm of rocking. A change in the mean impulsation frequency was noted only in expiratory neurons with constant rhythmicity.

Connection of the Labyrinth with the Sympathetic Portion of the Nervous System /242

The mechanisms of interconnections of the labyrinth with the sympathetic nervous system at the present time have still only begun to be studied, and only isolated facts on this question are present in the literature.

Megirian and Manning (1967) showed that in this case if stimulation of the vestibular nerve in cats preceded the stimulation of the nerves of the rear extremity by 190 msec, then responses to stimulation of the latter in the ipsilateral n. vagus and n. splanchnicus were completely absent. If the sequence of stimulations was reversed, then responses to stimulation of the vestibular nerve insignificantly decreased in n. vagus, and in n. splanchnicus they completely disappeared.

Hojo (1963) showed that after removal of the superior Cervical ganglions in rabbits, spontaneous and positive nystagmus appeared. Post-rotatory nystagmus after the operation decreased. The histological diagram immediately after the operation showed expansion of the vessels and edema of the labyrinth. In the latest periods edema disappeared but the changes in the vessels were preserved.

Jankowski et al. (1964) established that the sympathetic nervous system changes the microphone effect.

Spoendlin and Lichtensteiger (1966) histochemically defined noradrenalin in the sensory epithelium of the labyrinth. They established that there are two systems of adrenergic innervation of the sensory epithelium of the labyrinth: vegetative fibers, proceeding together with vessels and straight fibers. Experiments with section showed that the second system is of central origin. Adrenergic fibers were observed in the macula utriculus and in the cristae ampullaris and were not observed in the walls of the membranous labyrinth. The authors assume that adrenergic fibers correspond to nonmyelinized fibers of the vestibular nerves and that this system influences the sensitivity of the epithelium.

Ban (1964) studied the connection of the septo-preoptico-hypothalamic system with the vestibular nuclei. He separated this system into 3 regions: (1) parasympathetic regions which consist of the zone of the septum; the paraventricular preoptic zone and the paraventricular hypothalamic zone; (2) the sympathetic regions (medial preoptic zone and medial hypothalamus); (3) the parasympathetic zone (lateral preoptic zone and lateral hypothalamus).

The authors showed that the sympathetic region is closely interconnected with the vestibular nuclei through the dorsal /243
longitudinal bundle. In particular, through the dorsal longitudinal bundle, this region is interconnected with the vestibular component of the medial longitudinal bundle and thus an interconnection of vestibular nuclei with a sympathetic region through the interstitial Caljal's nucleus in the central gray matter is possible. Ban assumes that through these connections and the sympathetic regions there are sympathetic effects with stimulation of the labyrinth.

The mechanisms of the vestibular influences on the vegetative nervous system have just begun to be studied. The question of the

influences of electric stimulation of the vestibular nerve on the parasympathetic portion of the nervous system (n. vagus) have been studied. It was established that: responses in n. vagus to single stimuli of the vestibular nerve depend upon the activity of the respiratory center; vestibular activity has an influence on the activity of the respiratory center and on reflector discharges in n. vagus whereby on the latter is it significantly stronger; thresholds for activation of n. vagus are lower than for somatic systems; response reactions of n. vagus to stimulation of the vestibular nerve do not display the effect of temporal summation.

Much less studied are the mechanisms of interconnection of the vestibular analyzer with the sympathetic portion of the nervous system. However some of the data permit us to assume that the sympathetic effects are mediated by the septopreoptico-hypothalamic system.

CHAPTER VIII

CONNECTIONS OF THE LABYRINTH WITH THE RETICULAR FORMATIONS

Morphology

It is not known whether there are primary vestibular fibers to the reticular formation, but if they exist, there are few of them. The majority of the vestibuloreticular fibers are fibers of the neurons of the vestibular nuclei. /244

By the Naut method, degenerated fibers in cats were traced (Ladpli, Brodel, 1968) to the nuclei of the reticular formation with injury to each of the four chief vestibular nuclei. It was shown that the nuclei of the reticular formation providing ascending and descending fibers (giganto cellular reticular nucleus, a portion of the small cellular and caudal nucleus of the pons) received ipsi- and contralateral projections from the superior, lateral and descending vestibular nuclei. Moreover, protective zones correspond exactly to those regions of the vestibular nuclei which lead to the spinal cord and to levels above the spinal cord. Thus the vestibular nuclei, and likewise the fastigioreticular fibers, influence impulsation being sent by the reticular formation both in ascending and descending directions. The vestibuloreticular connections evidently are an important supplement to the fastigioreticular connections, acting as paths which mediate influences of the cerebellum to the reticular formation, insofar as the vestibular nuclei receive abundant afferentation from the cerebellum.

The lateral reticular nucleus (the nucleus of the lateral bundle), projecting onto the cerebellum, receives fibers from the ipsilateral Deiter's nucleus. The terminal regions of the fibers of Deiter's nucleus stretch in a rostral-caudal direction in the medial section of the reticular nucleus. It follows to note that other afferents to this nucleus of the reticular formation (afferents from the spinal cord, fastigial nucleus of the cerebellum, red nucleus, cortex of the brain) have sufficiently limited projection zones. If the terminal regions of each of the afferents are different, there is mutual overlapping between them, i.e., in the lateral reticular nucleus sending all its fibers to the cerebellum, and there are broad possibilities for interactions of impulses from various sources. Thus Deiter's nucleus, receiving broad afferenta-

tion from the cerebellum, may act on the cerebellum through the lateral reticular nucleus. /245

Another nucleus of the reticular formation projection to the cerebellum is the reticular nucleus of the mantle of the pons. This nucleus receives fibers from the contralateral superior and lateral vestibular nuclei chiefly in the ventral regions and also afferents from the superior tubers of the lamina quadrigemina and fibers of the brachium conjunctivum. Through the reticular nucleus of the mantle of the pons, Deiter's nucleus may indirectly influence the cerebellum insofar as this reticular nucleus sends its efferents to the cerebellum (Ladpli, Frodal, 1968).

Pompeiano and Walberg (1957) injured the cortex of the cerebral hemispheres, the basal nuclei and various portions of the mesencephalon in cats. It proved to be the case that the places where the fibers which descend to the vestibular nuclei originated were concentrated in regions of the mesencephalon near the central gray matter. After injuries of the cerebral cortex, Szentagothai and Raykovich (1968) observed degenerated fibers in the medial and the descending vestibular nuclei. All fibers to the vestibular nuclei lead from the medial longitudinal bundle and are terminal or preterminal. Degenerated fibers were found basically in the ipsilateral medial nucleus, especially its dorsal and caudal portions.

Basic fibers to the vestibular nuclei proceed from the region of the central gray matter, i.e., the mid-brain. Here three nuclei are differentiated: Cajal's interstitial nucleus, Darkshevich's nucleus and the nucleus of the rear commissure.

The straight interstitial vestibular tract was described by Lorente de No (1933a) and later by Pompeiano and Walberg (1957). In the last article it was demonstrated that the ipsilateral bundles of fibers from the interstitial nucleus to the vestibular nuclei passed downward in a medial direction from the medial longitudinal bundle in an oblique direction and ended in the medial vestibular nucleus. These fibers were both small and of average size. Injuries affecting Darkshevich's nucleus and the nucleus of the rear commissure, the inferior lamina quadrigemina and the reticular formation of the mid-brain did not affect terminal degeneration in the vestibular nuclei.

However, M. Shaybel' and A. Shaybel' (1962) described contralaterals of neuron-axons of the macrocellular nucleus of the bulbar pontile reticular formation which terminated in many regions of the brain including Deiter's nucleus, Darkshevich's nucleus and Cajal's nucleus.

The basic source of fibers going to the reticular nuclei can be considered to be Cajal's nucleus.

Physiology[10]

Vestibular Influences on the Reticular Formation

With stimulation of the vestibular nerve, Gernandt and coll. (1959) registered, in the reticular formation, three-phase and sometimes even more complex responses. These responses were not /246
discovered 2 mm below the bottom center of the fourth ventricle and 1 mm below the adjacent ipsilateral vestibular nucleus.

With registration of impulse activity Gernandt (1964) did not succeed in discovering connections between the deflection of the cupula in one direction or another and the rhythmic activity of neurons. Responses were observed which followed the rule of ampullofugal or ampullopetal current of the endolymph, but there might be a response reaction which did not follow this rule. This fact may be explained only by the fact that neurons are activated by contralateral canals.

After sectioning the eighth nerve it was possible to observe units reacting to stimulation of the contralateral labyrinth. These units were located in a limited region, which attests to the compactness of fibers from the contralateral labyrinth. A section of the brain along the central line 5 mm in length and 4-5 mm below the level of the vestibular nuclei completely eliminated response reactions to stimulation of the contralateral labyrinth.

Contralateral influence of the labyrinths through the reticular formation was also confirmed by data obtained with a study of Mautner's neurons (Retzlaff, 1957; Retzlaff, Fontaine, 1960). In this investigation it was shown that with unilateral stimulation of the roots of the eighth nerve, a powerful flexion of the caudal portion was observed, whereby the character of the response precisely reproduces the frequency of the stimulus. Bilateral stimulation of the roots of the eighth nerve did not elicit discharges from the two Mautner neurons which could be convincing, registering elicited potentials of the axons of these cells. A histological investigation conducted by the author showed that synaptic endings of the eighth nerve are located on dendrites and the cellular body of the ipsilateral Nautner neuron and on the axon pole of the contralateral Mautner neuron. Such a character of synapsis distribution agrees with the conception of the polar function of the neuron proposed by the authors. This conception asserts that afferent neurons which terminate on dendrites of the cellular body excite a discharge of the cells, but the fibers terminating on the axon monticulus or near it inhibit nerve impulse discharges. The endings of the fibers of the eighth nerve on the exciting pole of one Mautner cell and the inhibitory pole of the other influence, respectively, excitation and inhibition of opposite cells with stimulation of the eighth nerve. Endings of the eighth nerve not only enter into direct contact with the Mautner cells, but also are

[10]A number of questions in this section were dealt with in Chapters V and IX.

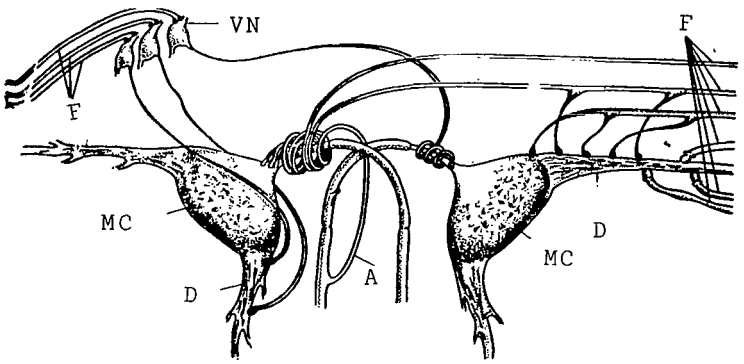

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Fig. 74. Mautner Cells and Their Connection with the Eighth Nerve. (A) Contralateral Axon from One Mautner Cell to the Axon of the Monticulus of the Other Ce ll; (B) Indirect Afference of the Eighth Nerve to the Mautner Cell (MC) Through the Vestibular Nerve (VN) Neurons of which in Turn May Synapse with Both Mautner Cells; (C) Direct Afference of the Eighth Nerve which Terminates in a Dendrite (D) of the Cellular Body of the Homolateral Mautner Cell, and Also on the Axon Monticulus of the Contralateral Cell (Retzlaff, Fontaine, 1960).

connected with them indirectly through neurons of the tangential nucleus and Deiter's nucleus, which comprise a complex of vestibular nuclei in fish. These two paths, direct and indirect, ensure the structural connections required for a powerful receptor response to sensory stimuli in fish. A direct receptor path of the third neuron arc consists of fibers of the eighth nerve of the Mautner neuron and motor cells of the spinal cord. Moreover, the author discovered the existence of axo-axon collaterals connecting both Mautner neurons. These branches arise from the axon of one Mautner neuron and after formation spiral around the proximal portion of the axon of the other, terminating on its axon monticulus. These collaterals play a feedback role, strengthening the effect of direct inhibition through synaptic endings of the contralateral nerve (Fig. 74).

The existence of axo-axon collaterals connecting both cells and differential staining of the dendrite region and the region of the axon monticulus, which changes the stimulus of the afferent fibers, is extremely important. Insofar as afferents of the eighth nerve are distributed in sufficiently specific regions along the two cells, and since it is impossible to elicit a discharge of the cells with simultaneous bilateral stimulation of the roots of the eighth nerve, it seems probable that the difference in cell staining is an indication of the inhibitory and exciting axons. Thus, in the system of the eighth nerve the Mautner cells of fish are two specialized cells which function as reciprocal elements whereby synaptic action changes the intracellular chemical state of the cells which leads either to excitation or inhibition.

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The Influence of the Reticular Formation on the Vestibular Nuclei

The influence of the reticular formation on the vestibular

nuclei was studied by Markham, Precht and Shimazu (1966). The basic intention of the authors in conducting the investigation was concentrated on the interstitial Cajal's nucleus.

Between the vestibular nuclei and Cajal's interstitial nucleus there are bilateral connections. Ascending connections are intersecting and non-intersecting. Descending connections are exclusively ipsilateral.

Stimulation of Cajal's nucleus elicits motions of the head in the horizontal plane and vertical and rotational motions of the eyes.

Eye motions elicited by stimulation of the vestibular apparatus are inhibited with stimulation of Darkshevich's nucleus, located besides Cajal's nucleus (Szentagothai, Schab, 1956; Scheibel, Markham, Koegler, 1961). Therefore the interest in studying the influence of Cajal's nucleus on the vestibular nuclei from the point of view of an analysis of the mechanisms of these eye motions is understandable. Experiments were carried out on non-narcotized cats under local anaesthesia; the cerebellum was removed. Electrodes for the stimulation of the reticular formation in Cajal's nucleus were introduced stereotaxically.

Stimulation was conducted by rectangular impulses with a duration of 0.1 msec amplitude from 1.1 to 10 V.

For identification of the types of vestibular neurons, the animals were subjected to rotation on a stand (cf. Chapter III).

Stimulation of the interstitial nucleus and structures 1-2 mm ventral of it elicited vertical connective eye motions, often accompanied by rotatory motions. With stimulation of other points of the mid-brain, eye motions were not observed.

Responses of the vestibular neurons were separated into three groups: (1) neurons were considered antidromically activating if they were activated with short latency (0.8 - 1.9 msec),had a constant latency with oscillations not greater than 0.5 msec and reproduced a rhythmic stimulation with an interval of 2-3 msec; (2) neurons were considered activating transynaptically if the latency of response was 2.2-9.5 msec and response reactions disappeared with rhythmic stimulation with an interval between the stimuli of 2-3 msec. Several neurons reacted to stimulations at frequencies of 1-3 imp/sec; however the majority reacted at frequencies of 30-50 imp/sec; (3) the action of neurons was considered inhibitory if their background rhythmicity decreased with a frequency of stimulation of 1-5 or 30-100 imp/sec. /249

Inhibitory responses were discovered in 41 of 44 Type I Cells of the vestibular neurons.

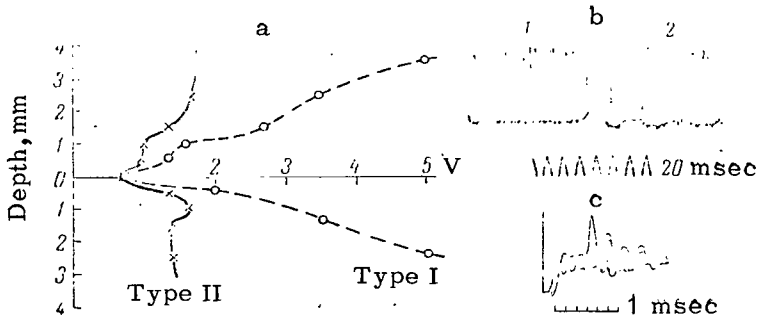

Fig. 75. Changes in Activity of Type I and Type II Neurons with Stimulation of Cajal's Nucleus. (a) Thresholds of Inhibition of the Vestibular Type I and Type II Neurons Thresholds Were Defined with a Frequency of 50 imp/sec; (b) Type I Neurons with High-Speed Spontaneous Rhythmicity at Rest (1) and (2) with Stimulation of the Ipsilateral Cajal's Nucleus at a Frequency of 6 imp/sec and Amplitude 5.8 V (50 Ray Superpositions). (c) Transynaptic Excitation of Type II Neurons with Stimulation of the Ipsilateral Interstitial Cajal's Nucleus at a Frequency of 3 imp/sec and Amplitude 2.0 V (Markham et al., 1966).

Type I neurons in different sections of the vestibular complex were inhibited with ipsilateral stimulation of the Cajal's nucleus (Fig. 75). If the stimulating electrode was located 1 - 3 mm dorsal or 0.5 - 1.0 mm ventral of Cajal's nucleus, either exciting responses were registered or the neurons did not react at all. Inhibition was discovered with a frequency of stimulation from 1 - 100 imp/sec. Usually the high frequency was more effective for obtaining the inhibitory effect.

The latency of inhibition was defined in neurons with high backgrounds of rhythmic activity which reacted to low frequency stimulation. Latency was relatively short (from 5 to 10 msec); in addition, the duration of the inhibitory effect (from 30 to 120 msec) depended on the size of the stimulus. Threshold values of the inhibitory effect equalled 1.2 $\pm$ 0.7 V.

Inhibitory effects were observed not only with stimulation of the central portion of the interstitial Cajal's nucleus but also /250 with stimulation of the rostral portion adjacent to the fasciculus retroflexis and caudal portions located in ventral and lateral directions from the nucleus of the third pair of cranio-cerebral nerves. Inhibition was developed even with stimulation of the medial and lateral sections of the interstitial nucleus, where significant differences in threshold values were not observed.

With stimulation of the ipsilateral Cajal's nucleus exciting

effects of the Type I vestibular neurons were not registered, with the exception of cases of a combination with inhibition noted above. Stimulation of the contralateral Cajal's nucleus elicited exciting influences upon the Type I vestibular neurons with mean threshold values of 1.3 ± 0.7 V. Transynaptic excitation was also observed with stimulation of a broad region of the mantle of the mid-brain. This region includes a larger portion of the reticular formation of the mid-brain, the red nucleus and part of the central gray matter. Thresholds of excitation of Type I neurons with ipsilateral stimulation equal 0.8 ± 1.1 of the contralateral 2.9 ± 1.2 V.

With stimulation of a more limited zone, including Darkshevich's nucleus and part of the reticular formation 1 to 2 mm lateral and ventral of the interstitial nucleus, threshold values were 1.6 ± 0.46 ipsilaterally and 1.7 ± 0.96 V contralaterally.

The latencies of transynaptic excitation fluctuated within the bounds of 2.2 - 9.5 msec; the range of oscillation increased with high-frequency stimulation. Approximately 10% of the neurons were discovered to have a 1:1 correlation between stimulus and response.

Antidromic activation was found in 10% of the cases with stimulation of the ipsilateral Cajal's nucleus, and 5% with stimulation of the contralateral nucleus.

In three neurons with stimulation of the ipsilateral Cajal's nucleus an inhibitory response reaction was registered, and with stimulation of the contralateral nucleus it was activated antidromically. These antidromic activating reactions were found with stimulation of all regions of the interstitial nucleus, including its rostral portions.

Thresholds of antidromic activity with stimulation of the ipsilateral nucleus equalled, on the average, 2.1 ± 0.96 and for the contralateral were 1.8 ± 0.96 V. The latency of responses was within 0.18 - 1.7 msec ipsilaterally and from 0.9 to 1.9 msec contralaterally. The distribution of these neurons in the vestibular nuclei was not defined.

The transynaptic exciting effect in Type II neurons was observed in stimulation of all regions of the ipsilateral and contralateral reticular formation of the mantle of the mid-brain (Fig. 81). In contrast to Type I neurons, cells were not found which would not react at all. Type II neurons were activated transynaptically with stimulation at high and low frequencies. Approximately 10% showed a 1:1 correlation between stimulus and response; the latency of responses in these cases fluctuated between 2.6 and 9.5 msec. The threshold of excitation with stimulation of the ipsilateral reticular formation of the mid-brain was on the order of 1.4 ± 0.76 V. The threshold of stimulation of the more lateral zones was the same. On the other hand, the case of the synaptic activation of

/251

of Type II neurons with stimulation of the ipsilateral Cajal's nucleus the threshold was 0.6 ± 0.5 V. Thresholds of transynaptic excitation of the vestibular Type II neurons with stimulation of the interstitial Cajal's nucleus were lower than thresholds of inhibition for Type I neurons (Fig. 75).

In one Type II neuron an antidromic exciting response was registered. The latency of response in this case equalled 0.9 msec. In four Type II neurons an unusual reaction was observed: with stimulation of the ipsilateral Cajal's nucleus their responses were inhibited in exactly the same way as in Type I neurons. The threshold values of current for these neurons was the same as for Type I neurons. Two of these neurons were distributed in the superior portion of the medial vestibular nucleus.

Neurons of the vestibular Type III nuclei were excited not only with access of angular acceleration in any direction, but also by stimulation by light, sound,touch and pressure to any portion of the head. Even several Type II neurons and sometimes Type I neurons revealed the same sensitivity to another form of sensory stimulation.

Type III neurons were activated transynaptically with stimulation of the majority of the regions of the mid-brain, including the interstitial Cajal's nucleus. Thresholds of stimulation for all regions were approximately the same and, on the average, equalled 0.8 ± 0.3 V. One Type III neuron revealed excitation with stimulation of all zones of the brain with the exception of the interstitial ipsilateral nucleus, with whose stimulation inhibition with a threshold of 0.18 V was noted.

With stimulation of the medial longitudinal bundle caudal of the interstitial nucleus and ventral of the nucleus n. oculomotorius, ipsilateral response reactions were similar to those which were observed with stimulation of the interstitial Cajal's nucleus: three Type I neurons were inhibited,(thresholds 1.0, 2.0 and 0.7 V) Type II neurons were excited transynaptically with lower threshold values (0.5 and 1.0 V). Thresholds of transynaptic excitation of Type II neurons with stimulation of adjacent regions of the reticular formation were 1.4 and 1.7 V. Stimulation of the reticular formation at a point 1.7 mm from the central line and lateral of the medial longitudinal bundle elicited inhibition in Type I neurons. Stimulation of the contralateral medial bundle elicited transynaptic excitation of Type I and Type II neurons. /252

With simultaneous stimulation of the medial longitudinal tubers by electrodes introduced into the bottom of the fourth ventricle caudal of the lower tubers of the lamina quadrigemina, inhibition in Type I neurons and in one Type II neuron was registered. After discovering a point which when stimulated, elicited inhibition, (this point was found in the interstititial nucleus), the ipsilateral medial was severed. All Type I neurons after section of the medial longitudinal bundle were activated with stimulation of the interstitial nucleus.

Thresholds of transynaptic excitation of Type II neurons were elevated after sectioning the medial longitudinal bundle. It is necessary to note that section of the medial longitudinal bundle changed neither the frequency of spontaneous impulsation nor responses to angular accelerations in Type I and II neurons. Incision of the gray matter in the caudal sections of the mid-brain did not change the effects of stimulation of the interstitial nucleus.

Thus stimulation of the reticular formation, and in particular of the interstitial Caljal's nucleus, was expressed in the form of two effects on the vestibular neurons: exciting and inhibitory. Stimulation of the ipsilateral interstitial Cajal's nucleus elicits inhibition in Type I neurons and ipsilateral transynaptic excitation in Type II neurons with significantly lower threshold values than with stimulation of the surrounding structures of the brain.

After section of the medial longitudinal bundles, stimulation of the interstitial nucleus does not elicit inhibitions in Type I neurons. Two types of connections are possible for these inhibitory influences on Type I neurons: antidromic through retrogressive collaterals, and orthodromic ones. Antidromic responses in neurons of the vestibular nuclei were bilateral, whereby contralateral responses were more pronounced since inhibitory influences of the interstitial nucleus were exclusively ipsilateral. This fact decreases the possibility of antidromic and recurrent inhibition. Ito and coll. (1964) also did not discover recurrent inhibition in Deiter's nucleus with stimulation of the spinal cord. Therefore it most probably follows to consider the orthodromic path of conduction of impulses through the descending fibers, described by Pompeiano and Walberg (1957), to be a unilateral interstitial vestibular tract.

Transynaptic excitation of the vestibular Type II neurons from the ipsilateral interstitial Cajal's nucleus with lower threshold values than the surrounding structures also disappeared after sectioning the medial longitudinal bundle, whereas sectioning did not influence the excitation of these same neurons from surrounding structures of the mid-brain. Therefore evidently axons of several neurons of the reticular formation of the mid-brain going into the medial longitudinal bundle did not terminate in vestibular nuclei (Pompeiano, Walberg, 1957). It is probable that fibers with which the transynaptic excitation of Type II neurons are connected also are fibers of the interstitial vestibular tract.

The explanation of the reason Type II neurons were excited and Type I inhibited by impulses conducted along the medial longitudinal bundle with stimulation of the interstitial vestibular nuclei evidently must be sought in the vestibular nuclei themselves. Shimazu and Precht (1966) showed that several Type II neurons may be intercalary inhibitory nerves which are activated by stimulation of the contralateral horizontal canal and elicit inhibitory influ-

ences on the homolateral Type I neurons (cf. Chapt. III). It is possible that descending impulses from the ipsilateral Cajal's nucleus excite several Type II neurons and the latter have an inhibitory influence on Type I neurons. This assumption corresponds to the fact that though the point of excitation of Type II neurons as well as the point of inhibition of Type I neurons are found in one territory in the mid-brain (i.e., in Cajal's nucleus), these influences are intermediated through the same path (i.e., the medial longitudinal bundle). The role of Type III neurons as inhibitory neurons was confirmed also by the fact that if discharges of Type II neurons are usually high frequency, then discharges of Type I neurons are poorly developed.

What is the significance of the ipsilateral inhibition of Type I neurons? The eye movements elicited by stimulation of the semicircular canal and electric stimulation of the vestibular nuclei are inhibited by stimulation of Darkshevich's nucleus (Szentagothai, Schab, 1956; Scheibel et al., 1961). At rest stimulation of Darkshevich's nucleus elicits a weakening of almost all eye muscles. If, however, Cajal's nucleus is stimulated, combined vertical and rotatory motions of the eye appear (Hassler, Hess, 1964; Toczek, 1962). Szentagothai and Schab (1956) consider Darkshevich's nucleus as an inhibitory center which influences the motor nuclei of the ocular muscles and Cajal's interstitial nucleus, the neurons of which have numerous synaptic endings in all motor nuclei of the eye muscles, with the exception of the nucleus n. abducens in that portion of the nucleus n. oculomotories which innervates the medial rectus muscle (cf. Chapt. IV), as an exciting center for vertical and rotatory eye motions.

Type I neurons which are probably important for horizontal eye movements and the tone of eye muscles, are neurons of the second order in the supposed two neuron chains between receptors of horizontal semicircular canals and neurons of the oculomotor nuclei. Probably inhibition of horizontal eye movements by the /253 ipsilateral interstitial nucleus facilitates vertical eye movements.

The interstitial nucleus and Darkshevich's nucleus receive projections from the pallidum (Johnson, Clemente, 1959) and from the striate cortex (Woodburn et al., 1946).

Ampullopetal current of the endolymph in the horizontal circular canal elicits excitation of Type I neurons and deflection of the eyes in the opposite direction (equivalent to the slow phase of nystagmus) and also leads to reciprocal excitation or inhibition of monosynaptic extensor and reflexor reflexes (cf. Chapt. V). But activation of the ipsilateral interstitial Cajal's nucleus has inhibitory influences on Type I neurons, which insure modulation of vestibulo-oculomotor and vestibulo-spinal systems of lateral movement of the eyes and trunk from the side of the higher centers.

These data attest to the fact that stimulation of the inter-

stitial nucleus ipsilaterally inhibits Type I neurons which are located in connection with the horizontal semicircular canals, but possibly even the Type I neurons which are connected with other semicircular canals are inhibited, as well as the neurons connected with the utriculus. If this is so, further investigations will indicate it.

CHAPTER IX

CONNECTIONS OF THE LABYRINTH WITH THE CEREBRAL CORTEX

The Cortical Projection of the Vestibular Analyzer

In studying the localization of specific structures of various analyzers, the method of elicited responses proved to be very fruitful. This method allowed the possibility of collecting large amount of factual material for establishing the cortical projection of the visual, auditory, sensomotor, olfactory, respiratory and visceral analyzers. /255

The experimental possibility of applying the method of elicited responses in relation to the vestibular analyzer was first shown in the research of Walzl and Mauntcastle (1949). In cats under light barbiturate anaesthesia the vestibular nerve, up to the point of its union with the auditory nerve, was stimulated with short stimuli. Also short-term mechanical stimuli of a fenestrated labyrinth were applied. Elicited responses with a latent period of 6-8 msec arose in the region adjacent to the forward portion of the focus sulcus suprasylvius. This region was bounded in the rear by the auditory, in the front by the somatic zone I, and ventrally by the somatic zone II. The projection is basically contralateral, but part of this region was activated even by stimulation of the ipsilateral nerve. Deepening anaesthesia strongly suppressed elicited responses to stimulation of the vestibular nerve while those to light sound and tactile stimulations were preserved.

Kempinsky (1951) conducted experiments using rotation and electrical stimulation of the 8th nerve of cats anaesthetized with nembutal. The nerve was stimulated bipolarly with impulses lasting 0.2 - 1 msec. Preliminarily (25 days earlier) the cochlea of the animals had been destroyed. After this time the cochlea nerve fibers had completely degenerated, insofar as even the cochlear ganglion, lying in the cochlea itself, was destroyed. The vestibular nerve fibers, in addition, remained more or less intact since scarpa's ganglion lying in the inner acoustic meatus was not injured. Elicited responses to stimulation of the vestibular fibers arose with a short latent period of 10-12 msec in g.g. supraectosylvii anteriorae bilaterally in both hemispheres. /256

Mickle and Ades (1952, 1954) electrically stimulated the visceral skin of the vestibular nerve in cats (nembutal anaesthesia). Elicited responses arose with a latent period of 6-8 msec in g.g. supra-ectosylvii anteriorae only in the contralateral hemisphere. The authors were able to trace the specific path of the vestibular apparatus, according to a list of responses, right up to the cortex. Stimulation of the nerve elicited responses in the ipsilateral vestibular nuclei with a latent period of 1-1.5 msec; in the contralateral portion of the midbrain lying ventral and lateral of the lower bigeminum, between the lateral and lower lemnisci with a latent period of 2.5-3 msec. In the diencephalon a small region (2 x 2 x 3 mm) was activated with a latent period of 405 msec lying forward and medial from the internal geniculate body and the border with nuc. ventralis posterolateralis thalamus.

Thus the vestibular path runs parallel to and directly adjacent to the auditory path.

Anderson and Gernandt (1964) in experiments on cats (dial anaesthetization, preparations of encéphale isolé or with decerebration at the precollicular level) stimulated in particular the ramuli of the vestibular nerve proceeding from the ampullas of the horizontal and vertical semicircular canals and also from the utriculus. Elicited responses arose in the forward portions of g.g. supra-ectosylvii of both hemispheres but stronger in the contralateral one. For the utriculus and each of the canals regions of maximum responses were found; these portions partially intersected (Fig. 76). Stimulation of a nerve of the ampulla of the horizontal semicircular canal elicited responses in portions of g.g. supra-ectosylvii anteriorae directly adjacent to the most rostral portion of s. suprasylvius anterior.

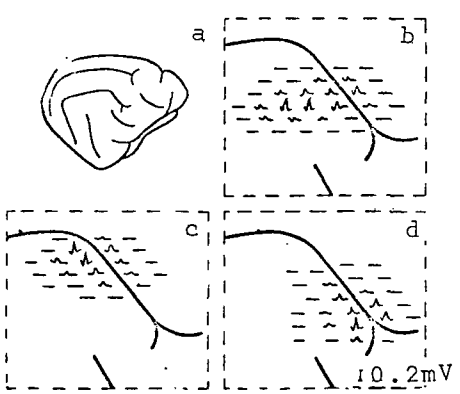

Fig. 76. Distribution of Cortical Potentials in the Right Hemisphere of the Cat in Response to Stimulation of the Ramuli of the Left Vestibular Nerve of the Utriculus (b), the Ampulla of the Forward Semicircular Canal (c) and the Ampulla of the Horizontal Semicircular Canal (d). Deflection of the Ray Upwards Corresponds to Electropositivity. (Andersson, Gernandt, 1954).

The focus of maximum responses to stimulation of the utricular nerve was distributed at the level of the midportion of s. suprasylvius anterior. Stimulation of the ampullar nerve of the forward semicircular canal elicited a more dorsal response at the level of the rear portion of s. suprasylvius anterior. /257

Massopust and Daigle (1960) stimulated the medial and descending vestibular nuclei in cats and kittens under nembutal anaesthesia with electrical impulses. Elicited responses arose with latent period of 8-10 msec in g.g. supra-ectosylvii anteriorae bilaterally, with the difference that the contralateral responses were of greater amplitude, and occupied a broader projecting region than in the ipsilateral hemispheres.

In the experiments of Grusser and coll. (1959) on nonanaesthetized preparations of encéphale isolé of a cat with the application of microelectrode technique, polarization of one labyrinth with a constant current activated neurons with a latent period of 8-20 msec exclusively in the contralaterally g. g. supra-ectosylvii anteriorae.

It is remarkable that stimulation of the vestibular complex (flocculo-nodular portion) above the cerebellum elicits primary responses with a latent period of 4-8 msec bilaterally in g. g. ectosylvii medialis (primary auditory zone) and g. g. supra-actosylvii anteriorae (Ruwaldt, Snider, 1956). However this complex probably does not participate in the appearance of elicited responses in these same regions of the cortex to stimulation of the vestibular nerve insofar as they are observed even after extirpation of the cerebellum (Mickle, Ades, 1954; Massopust, Daigle, 1960).

Kornhuber and Da Fonseca (1964), in analogous experiments, localized the vestibular projection in the regions of g. g. ecto-suprasylvius anteriorae bilaterally.

Spiegle and coll. (1965), stimulating the medial and lateral vestibular nuclei with rectangular impulses of electrical current, registered responses not only in g. g. ecto-suprasylvii anteriorae, but also from various regions of the thalamus and mid-brain (n. caudatus, putamen, globus pallidus, centrum medianum, the red nucleus, a macrocellular section of the medial geniculate body). With electrolytic damage to the rear group of nuclei of the macrocellular section of the medial geniculate body, including even the subgeniculate nucleus, responses in the investigated cortical regions and the caudal nucleus almost completely disappeared. Injury to the centrum medianum essentially decreased or eliminated response in the caudal nucleus (2/3 of cases), not changing responses in the anterior ectosylvian gyrus. Injury to the red nucleus in only one case weakened the response in the caudal nucleus and the stria pallidus system. Section of the medial longitudinal bundle and Forell's bundle and also section of the superior cerebellar peduncle along the chiasms did not noticeably influence the cortical responses of /258

the investigated regions. With several injuries in the midbrain, elevation of the amplitude of responses in the caudal nucleus were observed, on the basis of which the authors came to the conclusion of the possibility of existence, in the dorsal portion of the mantle of the mid-brain, of a system inhibiting responses of the fore-brain to vestibular stimulation.

Milojevic and Laurent (1966) stimulating the vestibular nerve of cats under chloralose anesthesia with electrical impulses (cochlear and facial nerves were severed) revealed two vestibular regions in the cortex: (I) the vestibular region in g.g. ecto- suprasylvii anteriorae; and (II) the vestibular region in the forward portion of g. ectosylvius posterior and the rear portion of the center ectosylvian gyrus. Responses in the rear ectosylvian gyrus had simple waveforms with small amplitude (0.2 - 0.5 mV) and a latent period of 12-16 msec, while responses in the forward and middle portions of the ectosylvian gyri had an amplitude of 0.8 - 1 mV and a latent period of 3-5 msec. Elicited responses of the contralateral side differed by the large amplitude and the number but not the latent period. With an increase in the frequency of stimulation, elicited potentials decreased in amplitude and disappeared; the same was observed under deep anesthesia with asphyxia and hypothermia of the animal.

Fredrickson and coll. (1966), in experiments on monkeys under nembutal anesthesia, registered cortical potentials elicited by electrical stimulation of the vestibular nerve of the posterior portion of the post-central gyrus at the bases of the intraparietal sulcus between the first and second somato-sensory regions (Fig. 77). Contralateral elicited responses had an amplitude of from 600 to 800 μV; ipsilateral responses were around 50 μV and extremely sensitive to anesthesia. The latent periods of ipsi- and contralateral responses were the same and equalled 5-6 msec. The authors also registered bilateral responses with approximately the same latency but of lower amplitude in the motor cortex in the anterior inferior portion of the centrallis sulcus. Responses in this region were more sensitive to the depth of nembutal anaesthesia.

The position of the cortical vestibular projection in monkeys between the first and second somatic regions is the same as in cats. However the overlap of the vestibular and auditory cortex which exists in the cat is absent in the monkey due to the broadening of the temporal and parietal regions and the development of a deep fissure of Silvins.

Thus with the aid of the method of the elicited potentials /259
the cortical projection of the vestibular analyzer was localized bilaterally in the cat in the anterior portion of the supra- and ectosylvian gyri according to the data of the majority of investigators. This region borders in the rear of the auditory, in the front of the somatic zone I and ventral of somatic zone II.

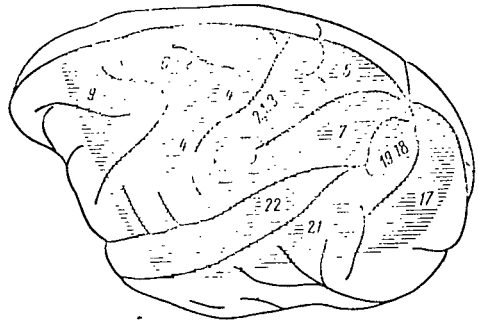

Fig. 77. The Vestibular Cortical Projection in the Monkey. Horizontal Shaded Area: the Investigated Regions of the Cortex with Stimulation of the Contralateral Vestibular Nerve; Black Spot: the Number of Responses 600 - 900 μV; Gray Spot: 300 - 600 μV; White Spot: 0 - 300 μV. The Numbers are Broadman's Regions (Fredrickson, et al., 1966).

In primates (monkeys) the cortical projection of the vestibular analyzer is also located between somatic zones I and II, but due to the characteristics of the development of specific regions of the cortex probably in Broadman's second region.

The question of the existence of the secondary vestibular projection, the presence of which is characteristic of the visual and auditory analyzers, remains unclear.

As before very little is known about the projections of the nonauditory labyrinth to the subcortical regions of the more cranial oculomotor nuclei.

Reactions of Various Regions of the Cortex in the Subcortical Formation to Adequate Stimulation of the Vestibular Apparatus

Changes in Summary Bioelectrical Activity of the Cortex of the Cerebral Hemispheres and Several Subcortical Formations with the Action of Angular Acceleration

In this and subsequent sections we will introduce the results of our own investigations of the changes in bioelectrical activity of the cortex of cerebral hemispheres and the subcortical formations with the action of angular and alternating linear accelerations in experiments on cats (we tried to show the peculiarities of reactions of various zones of the cortex of animals with a more differentiated cortex).

Experiments were conducted on 14 cats and 10 rabbits weighing /260 2-3.5 kg.

The bioelectrical activity in cats (anterior ectosylvii and suprasylvian gyri of the visual and motor zones, and of the frontal lobes) and also the activity of the sensomotor zones of the cortex of rabbits were investigated with the aid of needle electrodes introduced into the vault of the skull directly before the beginning of the experiment.

The study of changes in bioelectrical activity of subcortical structures (the reticular formation of the mid-brain at the level of the tuber of the forward lamina bigeminum, of the posterior hypothalamus and the hippocampus) was carried out with the aid of nychrome electrodes with a diameter of 30 - 50 μ, covered with a vitreous solution up to the tips. Electrodes were forced into the rabbits after 7 - 10 days and introduced into the cats under light ether anesthesia 3 - 6 hours before the experiment.

Electrodes were introduced into openings in the skull bored with an electric drill: for the cats, according to Szentagothai's coordinates (1957) and for the rabbits, according to the coordinates of Sawyer et al, (1954).

After the experiment the animals were killed and the location of the tip of the electrode was controlled histologically. Preparations were tinted with hematoxilin eozine. The point of registration of the cortical zone in the cats was determined visually according to the atlas of Jasper and Aimone-Marsan (1954).

Recording the biopotentials was done bipolarly and monopolarly on a recording electroencephologram made by the Kaiser Laboratorium.

In part of the experiment (5 cats, 10 rabbits) for evaluation of the general condition of the animal an EKG and respiration rate were observed.

Transmission of biopotentials to the electroencephalograph was made through silver collector rings.

Before the experiment the animal was fixed in an immobile position in the frame of a stereotaxic instrument set on a platform of a rotating apparatus with two degrees of freedom (Fig. 78). The control panal allowed us to change the direction of rotation and speed of rotation of the platform in the horizontal plane from 30 - 150 °/sec, and in the sagittal from 1 - 5 °/sec.

During the experiments the animal was covered with a screening net. Experiments were conducted in light. The bioelectrical activity of the investigated formations was registered during acceleration which always lasted for 6 seconds before the given angular velocity (30, 48 and 60 °/sec) during rotation at a constant speed in a horizontal plane, with inclinations of the platform in the sagittal plane, with rotation in the horizontal plane with and without a reverse, in the horizontal plane with simultaneous inclinations in the sagittal plane.

Immediately after cessation of rotation (stop stimulus) bio- /261
potentials of the residual effect were registered for 1-1/2 minutes, further after 5, 10, 15, 20, 40, 60 and 90 min. The duration of each recording was 20 - 30 sec.

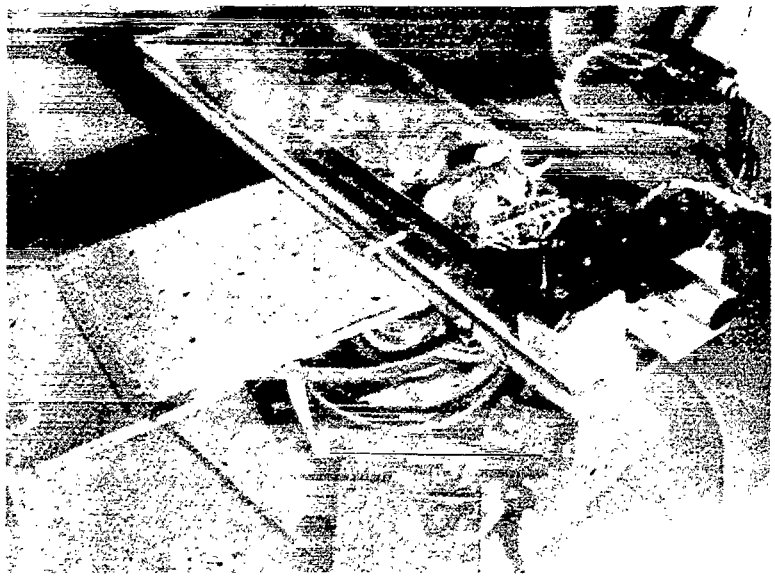

Fig. 78. Cat on Rotation Stand

Amplitudes of biopotentials of different zones of the cortex of the cerebral hemispheres in the cats equalled 120 - 200 μV at rest; the frequency of rhythms were from 1 - 3 to 20 Hz and higher. Slow rhythms of 1-2 Hz in amplitude to 200 μV were pronounced on recordings of the frontal and parietal lobes, the ecto- and suprasylvian gyri. They might be a consequence of the anesthesia, although the latter was not deep (all reflexes were preserved). Characteristic for the recordings of various zones of the cortex in the cat (except for the frontal removals of charge) were bursts of rhythm with a frequency of 10 - 11 Hz, similar in character to alpha-rhythm discharges in man which were not observed in the rabbits.

Initially, in rabbits and cats, on the recording of the hypothalamus rhythms of 6-8 Hz and 50-70 μV predominated. Also even slower rhythms of 1-2 Hz with an amplitude of 100 μV and higher were noted. On recordings of the reticular formation, rhythms of 1-2 Hz predominated, and in those of the hippocampus, slow oscillations.

During acceleration and the beginning of rotation in the horizontal plane with a velocity of 30 °/sec the frequency of heartbeat and respiration increased, and on electrocorticograms (EKOG) a desynchronization reaction was observed, especially pronounced during the first 10 - 15 sec of rotation. The level of biopotentials was lowered to 20 - 80 μV. On recordings of the frontal removals of 5 - 10 sec of rotation the original pattern (predominance of slow waves) was restored. According to the duration of rotation, the level of biopotentials was elevated to 60 - 120 μV, on the average, /262

but never reached the original value. The number of rhythms of 1-3 Hz decreased and those of more than 15 Hz increased. Bursts of rhythm of 10 - 11 Hz significantly decreased in duration (to 1 sec) and amplitude (50 - 60 μV instead of 100 μV before the activity). After stopping the stand the bioelectrical activity was quickly restored to the original level with a duration of rotation of 5 min (Fig. 79), and only after 15 min with a duration of rotation of 1 hour.

Changes in rhythms in rabbits had a synchronized nature. The latter was apparent on recordings of all removals of charge. On recordings of removals of charge from the cortex it was also possible to note an increase in frequent rhythms. In the cortical formations the synchronization phenomena were pronounced due to the increase in rhythms at a frequency of 6-8 Hz. The number of rhythms of 1-2 Hz decreased. As a consequence, in 6 rabbits it was possible to note an elevation in voltage of these rhythms (to 100 - 120 μV in several animals), while during rotation the amplitude of these rhythms was 50 - 80 μV.

In the first 6 - 10 seconds from the moment of rotation at a speed of 48 °/sec, rhythms of 3 - 3.5 Hz and of high amplitude (100 - 150 μV) appeared on the EKOG. Gradually the amplitude of these rhythms during rotation lowered to 80 - 100 μV and after 2 - 3 minutes of rotation slow and superslow rhythms (1 and 0.5 Hz) appeared. These rhythms were equally pronounced on recordings of all removals of charge from the cortex, and it is difficult to determine where they first appeared. During the first 6 - 10 sec after stopping the stands, high voltage rhythms at a frequency of 3 - 5 Hz also were noticed, which gradually disappeared and were replaced by more frequent rhythms (up to 8 - 10 Hz) of lower voltage, so that the character of activity is similar to the pattern during rotation. However it was impossible to note a pronounced desynchronization reaction (Fig. 80c, 5-6th channels). After rotation for 5 minutes, the electrical activity was restored in 3 - 5 minutes; after rotation for an hour, in 15 - 20 minutes.

During acceleration up to a speed of 60 °/sec, slow rhythms of 1 - 2 Hz (more pronounced in cats) with an amplitude of 200 μV immediately appeared on recordings of all removals. A 3 - 3.5 Hz voltage of rhythms increased to 200 μV, where upon a certain shift in the frequency of rhythm to 4 - 4.5 Hz, the amplitude of which gradually lowered to 60 - 80 μV, was noted. Then the synchronized rhythms of 6 - 8 Hz (more pronounced in rabbits; Fig. 81) became predominating.

The presence of 4 - 4.5 Hz rhythms in the first seconds of rotation and their replacement by 6 - 8 Hz rhythms was characteristic of recordings in the subcortical formations (Fig. 81). In cats, as opposed to rabbits, in addition to the above-described changes in the form of synchronization of rhythms in the posterior hypothalamus, reticular formation alpha-type rhythms (8-10 Hz) were registered in

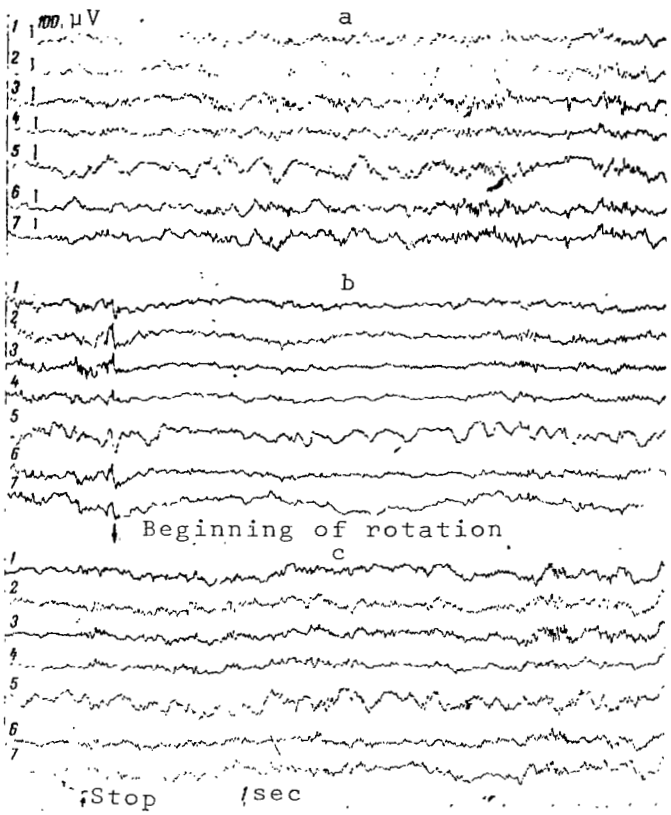

Fig. 79. Changes in Bioelectrical Activity of the Cortex of the Cerebral Hemispheres Under the Action of Angular Acceleration in the Horizontal Plane (Speed of Rotation: 30 °/sec; Duration of Acceleration: 6 sec). (a) Original Pattern; (b) During Activity; (c) Period of Residual Effect. (1) Ectosylvii sulcus; (2) Left Sylvii Gyrus; (3) Left Occipital Region; (4) Right Parietal Region; (5) Left Frontal Region; (6) Right Ectosylvii Gyrus; (7) Right Occipital Region. /263

the cortex. With rotation the amplitude of their discharges increased to 250 μV and the number of such pulses of alpha-type rhythms increased. The amplitude of these rhythms rose especially during the period of the residual effect. In one cat it reached 300 μV. According to the degree of restoration of the original value the alpha-rhythm disappeared. After stopping the stand, aside from an increase in the rate of respiration and heartbeat it was possible to visually observe a very clear nystagmus in the animals.

With rotation in the horizontal plane at a speed of 80°/sec with reverse (Fig. 82), during the period of turning, a significant lowering of amplitude of the rhythm to 50-100 μV (desynchronization reaction) was observed. Alpha-type rhythms in cats disappeared. Rhythms of 1 - 2 Hz in amplitude up to 100 - 120 μV were pronounced; the number of swift rhythms above 15 Hz decreased.

After cessation of rotation, if it was not extended (shorter than 5 minutes), the pattern of the rhythms comparatively swiftly returned to the original. However, in cats in the residual effect period, discharge rhythms of 8 - 10 Hz with an amplitude up to 200 μV (Fig. 82) were registered.

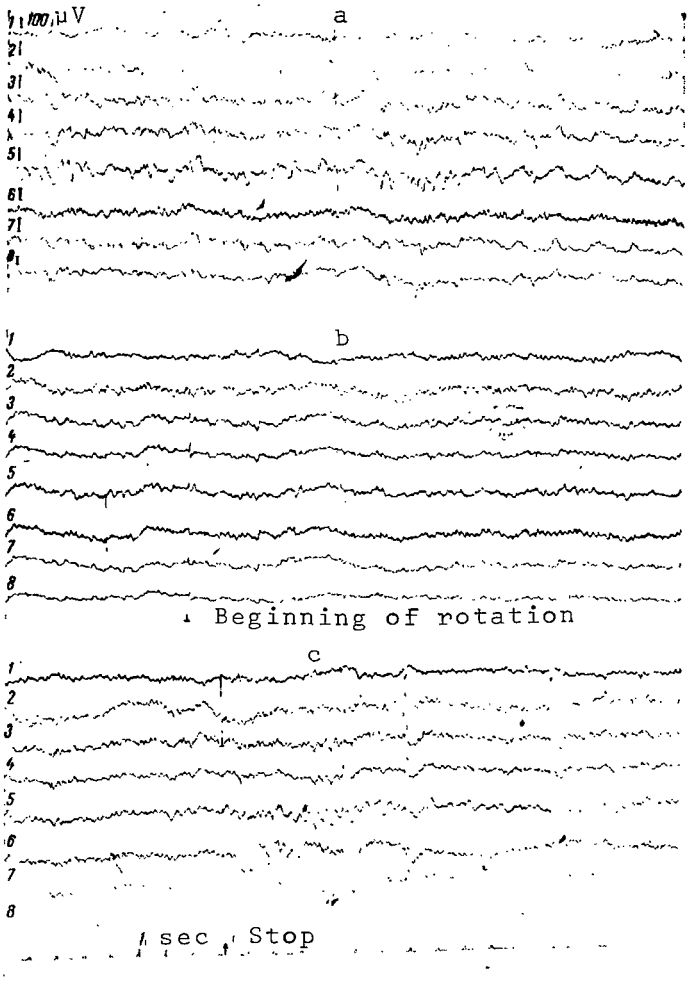

Fig. 80. Changes in Bioelectrical Activity of the Cortex and Subcortical Formations With the Action of Angular Acceleration in the Horizontal Plane (Speed of Rotation: 48 °/sec). /264
(1) Posterior Hypothalamus (Right Half); (2) Hypothalamus (Left Portion); (3) Reticular Formation (From the Right); (4) Hippocampus (Right Hemisphere); (5) Cortex of the Sensomotor Zone of the Right Hemisphere; (6) Cortex of the Sensomotor Zone of the Left Hemisphere; (7) Reticular Formation (From the Left); (8) Hippocampus (Left Hemisphere). Bipolar Removal. (a-c). The Same as in Figure 79.

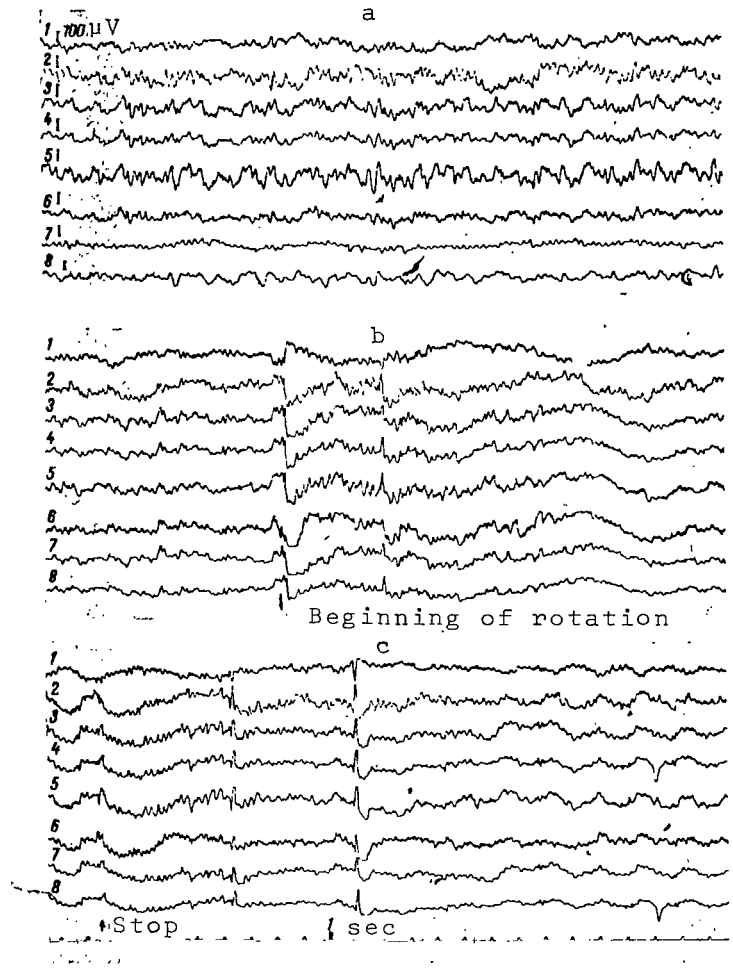

Fig. 81. Changes in Bioelectrical Activity of the Cortex and Subcortical Formations Under the Action of Angular Acceleration in a Horizontal Plane (Speed of Rotation: 60 °/sec). /265
(a-c). The Same as in Figure 79.
(1) Reticular Formation (From the Right); (2) Posterior Hypothalamus (Right Region); (3) Hypothalamus (Left Region); (4) Reticular Formation (From the Left); (5) Cortex of the Right Hemisphere; (6) The Same with the Left; (7) Hippocampus of the Right Hemisphere; (8) The Same of the Left Hemisphere. Bipolar Removal of Charge.

With rotation at a velocity of 60 °/sec at the beginning of each rotation it was possible in all removals of charge to observe a short-term appearance of 4 - 4.5 Hz rhythms for 2-3 sec. Further, a pattern of rhythms of lowered voltage was registered. After stopping, discharges of 8 - 10 Hz rhythms with a high amplitude were registered in cats. However they were manifested somewhat later at the end of the first or at the beginning of the second minute of the period of residual effect on a background of lowered amplitude of rhythm. If rotation with reverse was continued for 40 - 60 minutes, then restoration of the original pattern was observed after 2 - 2.5 hours. /266

The original pattern was observed even with inclinations of the animal in the sagittal plane. It was expressed in desynchronization of rhythms; the level of voltage was lowered to 70 - 100 μV (Fig. 83). Such a picture was observed in all tested zones of the cortex. The appearance in the upper rotation point of discharges of frequency of 8 - 10 Hz and an amplitude of 200 - 250 μV lasting for 3 sec was characteristic for cats. In a less expressed form, these changes were registered in the lower rotational point (Fig. 83b). With inclinations of the cat in the sagittal plane, even alpha-type rhythms of 1 - 2 Hz predominated, as did synchronized rhythms of 6 - 8 Hz (in rabbits). As a consequence the original activity was restored quickly (in 10 - 30 seconds) even if changes of the animal's position were long (up to an hour). In the first seconds of residual effect in cats, it was possible to note the appearance of discharges of 8 - 10 Hz in the rhythm of motion of the stand (of inclination of the platform). During the residual effect period, the number of alpha-rhythms increased in the cats.

With inclinations of the animal in the sagittal plane and simultaneous horizontal rotation, discharges of the rhythm of 8 - 10 Hz with downward movement of the head of the animal from the upper point of elevation was not expressed as clearly as when the platform was turned without rotation. The voltage of rhythms was somewhat lowered.

In the subcortical formations, rhythms of 6 - 8 Hz up to 70 - 80 μV in amplitude and also lower rhythms (1 - 2 Hz) up to 100 μV in amplitude were registered.

With rotation in the horizontal plane with a reverse and simultaneous inclinations of the platform, changes were expressed in lowered voltage of basic EEG rhythms. Discharges of rhythms of 8 - 10 Hz were rarely found, and if they were detected, then their amplitude was significantly lowered. On recordings of subcortical formations, a significant lowering in the voltage of the rhythms (to 60 - 80 μV) was noted. Rhythms of up to 4 - 4.5 Hz at the beginning of each appearance were registered for 4 - 5 sec.

In general, changes in bioelectrical activity with rotation in the horizontal plane with and without a reverse and of simultaneous

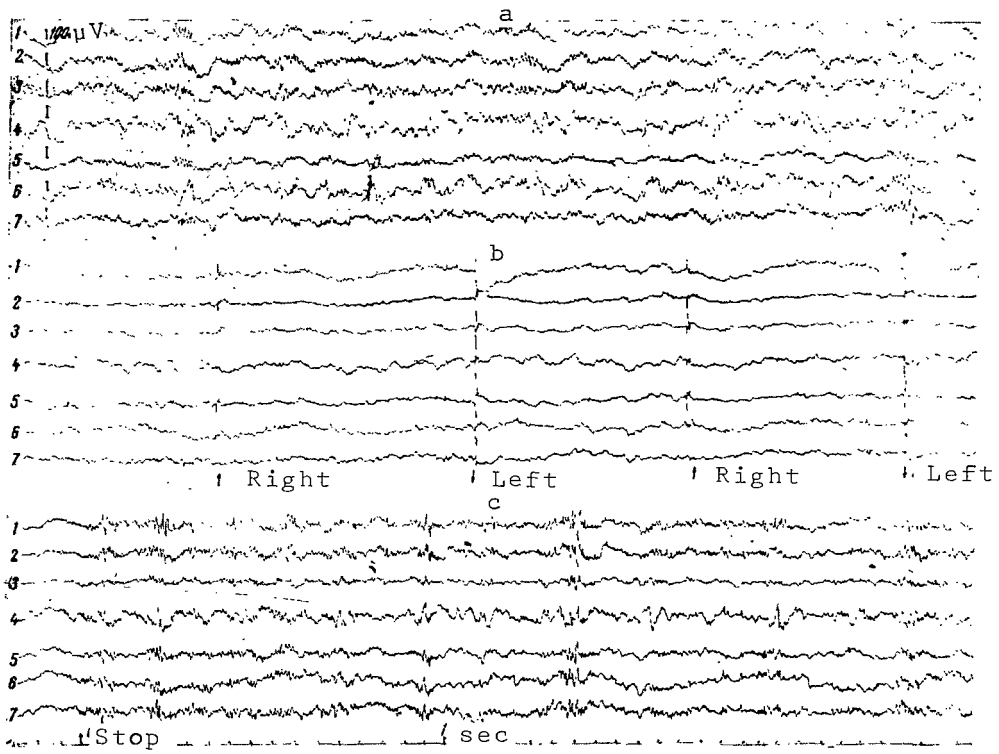

Fig. 82. Changes of Bioelectrical Activity of the Cortex of the Cerebral Hemispheres with Rotation in the Horizontal Plane With Reverser (Speed of Rotation: 48 °/sec). /267

Designations the Same as on Figure 79.

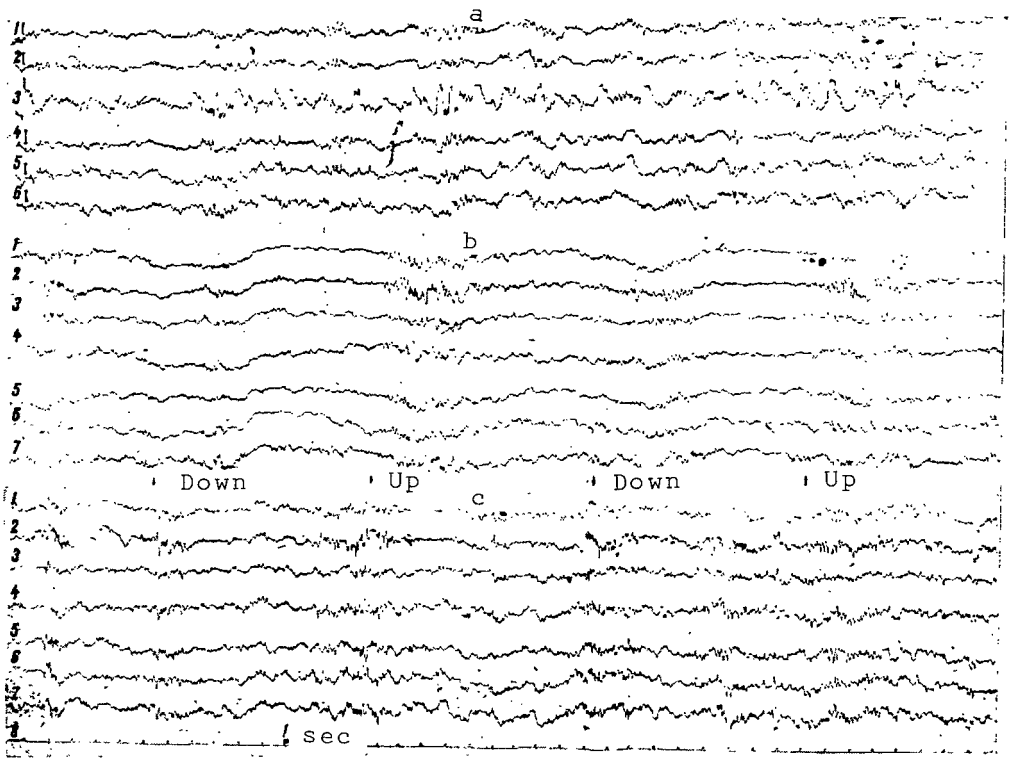

Fig. 83. Changes of Bioelectrical Activity of Various Zones of the Cortex With Inclinations of the Platform (Head Down-Up). /268

Designations the Same as on Figure 79.

inclinations of the platform had a mixed nature, but changes characteristic for rotation in the horizontal plane predominated. This /269
evidently is connected with the limited range of velocity (1 - 5 °/sec) of inclinations of the platform in the sagittal plane.

Thus the character of changes in bioelectrical activity of various zones of the cortex depends upon the amount of acceleration. Changes in the activity of subcortical formations with the action of angular accelerations is characterized by a lowering of the amplitudes of the basic rhythms and the appearance, rather, of an increase; rhythms of 6 - 8 Hz dominate on recordings of all subcortical formations over frequencies of 1 - 2 Hz. At the moment of the beginning of rotation in the horizontal plane with speeds of 48 and 60 °/sec, in both formations, as in the cortex, rhythms of 4 - 4.5 Hz of high amplitude are registered during 5 - 6 sec.

With the aim of clarification of the genesis of the observed changes in activity in the cortex and also of the exclusion of artifacts connected with the movement of blood in the vessels of the brain at the beginning of rotation and after stopping the stand, we investigated the biopotentials of the cortex on preparations of cerveau isolé (3 rabbits). A section of the brain in animals was made in front of the lamina quadrigeminum.

After sectioning the brain stem, on recordings registered both mono- and bipolarly, waves with a frequency of 1 - 2 Hz characteristic of preparations of cerveau isolé were observed, as well as super-slow rhythms (0.5 - 0.3 Hz) of high amplitude (200 - 250 μV). Neither rotation in the horizontal plane nor inclinations of the path of platform in the sagittal plane nor simultaneous motion in both planes with a reverse in the horizontal plane and without it, changed the original picture. The fact is curious that rate of respiration and heartbeat also did not change (Fig. 84). It is possible to suppose that changes in cardiac activity and respiration are connected with influences of the above-lying structures, and also that the duration and phase level of changes arising in different regions of the brain in the experiments were conditioned not only by adequate stimulation of the vestibular apparatus, but also by the involvement of other mechanisms; in particular, of the nonspecific formations of the brain stem.

Insofar as these experiments were conducted on rabbits, we could not establish the genesis of alpha-type discharges observed in the cortex of the cerebral hemispheres of cats. However on the /271
basis of experiments with an isolated sphere of the cortex (MacLean et al. 1965), it is possible to assume that they are connected in origin with nonspecific structures.

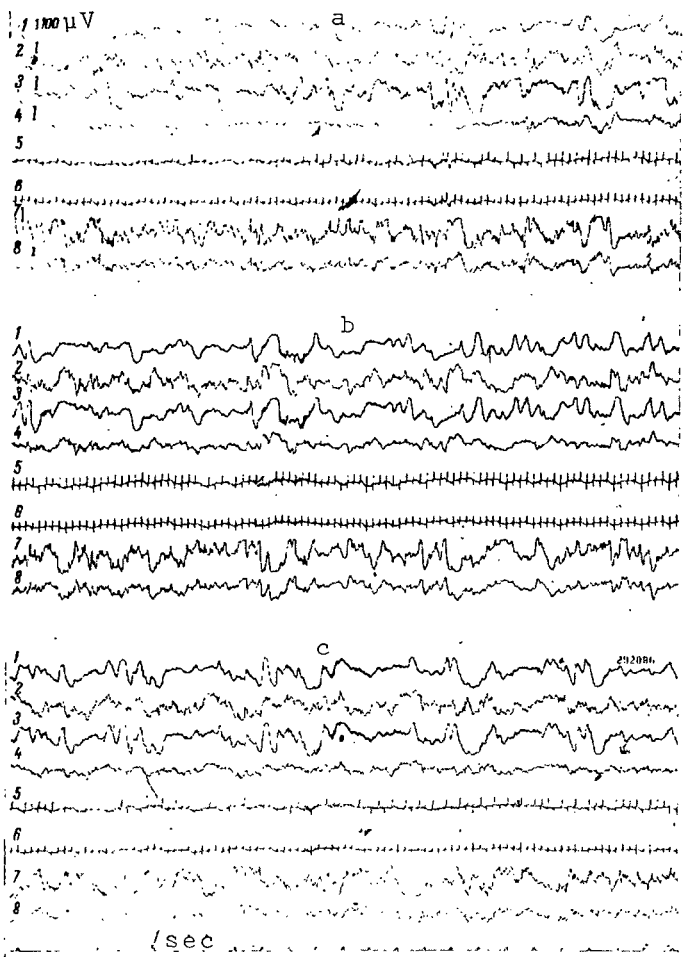

Fig. 84. Bioelectrical Activity of a Cerveau Isolé Preparation with the Action of Angular Acceleration in a Horizontal Plane. (Speed of Rotation 60 °/sec). /270

(a-c). Same as in Figure 79.

(1) Visual Zone of the Left Hemisphere, Monopolar Recording; (2) The Same of the Right Hemisphere; (3) Motor Zone of the Cortex of the Left Hemisphere Monopolar Removal; (4) The Same of the Right Hemisphere; (5, 6) EKG, 1st and 2nd Removal of Charge; (7, 8) Bipolar Recording of the Left and Right Hemispheres.

Changes in Summary Bioelectrical Activity of the Cortex of the Cerebral Hemispheres and of Several Subcortical Formations with the Action of Alternate Linear Accelerations

Experiments were conducted on 7 cats. Introduction of electrodes in the region of the vestibular nuclei was made along Szentagothai's coordinates (1957). Electrodes were introduced in the cortex of the cerebral hemisphere in the region of the anterior margins of the ecto- and suprasylvian gyri. Removal of charge was monopolar. A passive electrode was attached under the skin of the frontal nasal portion of the skull. The activity was registered on the recording electroencephalograph of the Elther Co. The amplitude of vertical movements of the platform of the stand varied within 350 - 550 mm. Frequency of oscillations was regulated from 30 - 50/min.

A flight stimulus was applied as a functional load. Light stimuli at a frequency of 18 flashes/sec were given from a photostimulator made by the Elther firm.

With the transmission of the light stimulation, the recordings of the cortex from the regions of the ecto- and suprasylvian gyri indicate undecipherable adaptation of the rhythm of light flashes. In the reticular formation and the vestibular nuclei these light stimuli did not elicit any apparent changes in biopotentials (Fig. 85a).

From the very beginning of rocking, in all investigated regions of the brain a shift toward high frequencies was observed. The amplitude of rhythm of 18-25 Hz increased to 80 - 120 μV. Slow oscillations (3 - 5 Hz) disappeared. On this background, light stimulus elicited a clear reaction of rhythm stimulation which appeared not only in the cortex, but also in the reticular formation of pons Varolii. The amplitude of potentials elicited by light reached 130 - 170 μV (Fig. 85d). Similar changes were observed throughout rocking (30-40 min).

G. I. Gorgiladze and G. D. Smirnov (1964), with stimulation of the cat's eye by light pulses with a rhythm of 10-15/sec, noted that after certain time, in the cortex the amplitude of responses falls and individual responses are separated out (transformation of rhythm). With polarization of the labyrinth, responses were not only completely restored but even increased in comparison to the original. Such an easing in the reaction was observed even with electrical stimulation of the reticular formation. After stopping the stand, even in the first minute it was possible to observe restoration of slow rhythms at a frequency of 3 - 5 Hz and an amplitude of 80 - 100 μV. These rhythms were registered both from the cortex and the subcortical formations which we investigated. Light stimuli during the first 5 minutes after cessation of rocking continued to elicit adaptation reaction of rhythm both in the cortex and in the reticular formation of the mid-brain, although not to such a degree as with rocking (Fig. 85b).

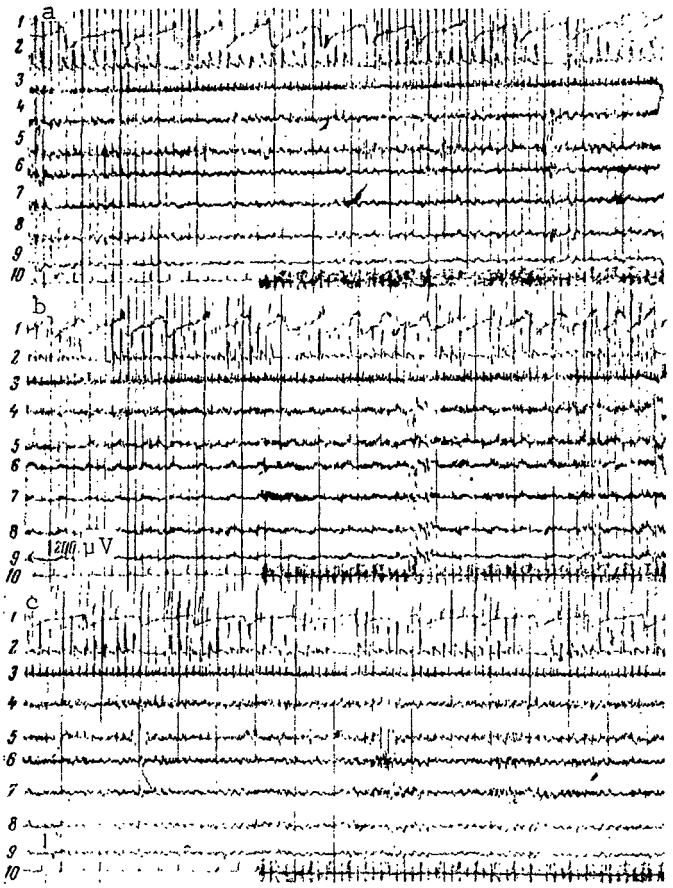

Fig. 85. Changes of Bioelectrical Activity in the Cortex of the Cerebral Hemispheres (Anterior Margin of the Suprasylvian and Ectosylvian Gyri), Reticular Formation of the Pons and Regions of the Vestibular Nuclei with Rocking. (a-c) Same as in Figure 79. (1) Respiratory Motions; (2) Analysis of the Spectrum of the Frequencies of the 6th Recording; (3) EKG; (4) Biocurrents of the Cortex of the Right Hemisphere; (5) The Same of the Left Hemisphere; (6) Reticular Formation (from the Right); (7) The Same from the Left; (8) Zones of the Vestibular Nuclei (from the Right); (9) The Same from the Left. (10) Time Notation and Signal of Light Stimulation. /272

Thus general changes, which we observed even with simultaneous /273
registration of bioelectrical activity of the cortex of the brain, in the reticular formation of regions of the vestibular nuclei during rocking led to the appearance of a shift in frequency to the side of the reaction of biopotential desynchronization in all investigated formations. These changes were continued throughout the test and began immediately with the beginning of the rocking. On a background of desynchronization reaction, as is known from the work of Marsuyeva and Chistovich (1954) and Ziglina and Novikova (1962), in the cortex and reticular formation the reaction of assimilation of the rhythm of an exteroceptive stimulus is significantly facilitated. A similar effect was observed even in our experiments.

The following fact is of interest. In the residual effect toward the end of the first minute or the beginning of the second, spindle-shaped discharges with a frequency of 7 - 9 Hz and an amplitude up to 400 μV appeared in the cortex, increasing in value with time and gradually propagating to the underlying regions. In shape they are similar to discharges which we registered with horizontal rotation (during residual effect) and with inclinations of the platform (cf. preceding section), but were more clearly pronounced (Fig. 86). Toward the 10th - 20th minute these discharges were registered in all investigated regions. Their amplitude at this time reached 600 - 700 μV. Simultaneously an increase in the amplitude and number of slow waves was observed. Toward the 30th-35th minute after cessation of rocking the discharges disappeared and the pattern of bioelectrical activity approached the original.

G. V. Izosimov conducted experiments, in which rabbits were rocked, parallel with our own. In the aim of comparing the material obtained by us with data on the rotation of rabbits and to analyze changes in the cortex with rocking, we shall deal with these in somewhat greater detail.

Experiments were conducted with 30 rabbits. Rocking was prolonged (1 hr); the amplitude of rocking was 50 cm. Five rabbits of this group had electrodes introduced into the reticular formation and the posterior hypothalamus. Registration of biopotentials was made after stopping the stand: after 15, 30, 40 and 60 minutes of rocking.

Fifteen minutes after the beginning of rocking, in most of the animals an increase in slow activity was noted and the swift components, as a rule, disappeared or their number and amplitude significantly decreased (Fig. 87). In the reticular formation of the mid-brain and the posterior hypothalamus a lowering of the amplitude of the basic rhythm (5-6 Hz) is observed during these periods. Moreover, in the reticular formation a strengthening of superslow rhythms was noticed.

After 30 minutes of rocking, slow rhythms of bioelectrical activity of the cortex were still more strengthened; the amplitude

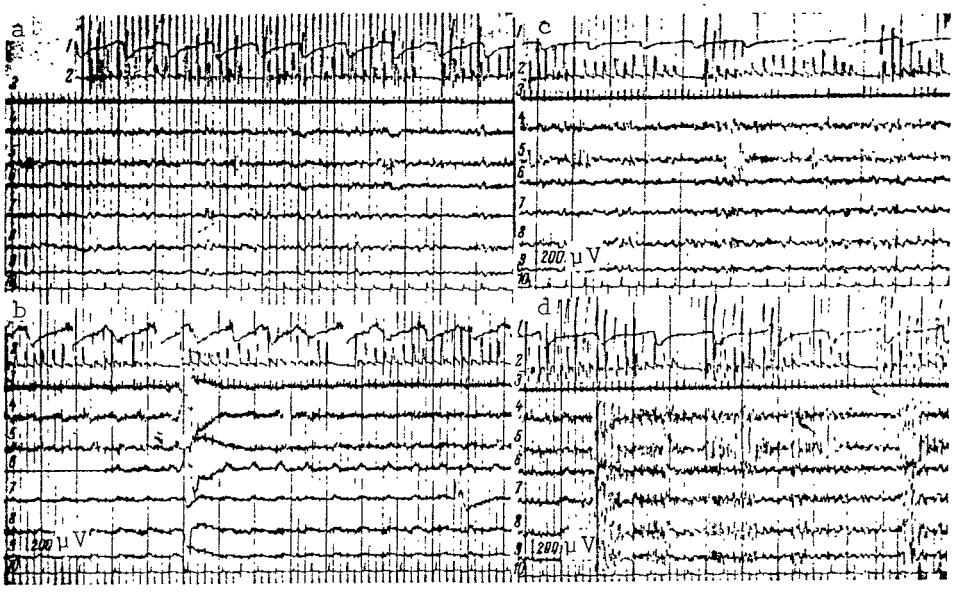

Fig. 86. Changes in Biopotentials of the Cortex of the Reticular Formation and Regions of the Vestibular Nuclei with Rocking. Designations the Same as on Fig. 85. (a) Before the Activity; (b) During the Activity (the Artifact from the Motion of the Animal and Mechanical Artifacts from Displacement of the Conducting Leads During Rocking Are Seen); (c,d) 1st and 20th Minute of Residual Effects. /274

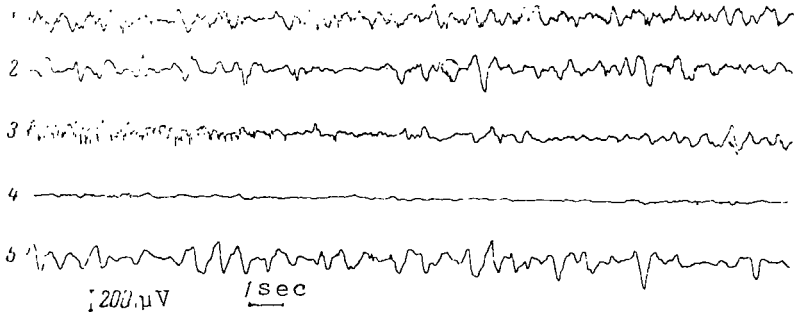

Fig. 87. Changes in Bioelectrical Activity of the Cortex of the Cerebral Hemispheres in Rabbits with Prolonged Rocking. (1) Before the Activity; (2,3,4) Respectively, after 15, 45, 60 Minutes of Rocking; (5) 30 Minutes After Cessation of Rocking (According to Izosimov). /275

of superslow oscillations in the reticular formation was increased; superslow rhythms appeared even in the hypothalamus.

In the 45th minute of rocking in the cortex epileptiform discharges were observed (Fig. 87). In the reticular formation in the hypothalamus, superslow oscillations were still more increased, and the amplitude of the basic rhythm (5-6 Hz) was lowered.

In the 60th minute of rocking, in 22 rabbits the recording of bioelectrical activity of the cortex showed that slow rhythms completely disappeared. At these times only separate surges of high frequency activity (18-20 Hz) of not more than 10 - 15 μV were recorded against a background of full extinction of activity (Fig. 87). In 8 animals, individual sections of high amplitude slow waves were still apparent. In the reticular formation in the hypothalamus, a depression of activity also developed. Restoration took place gradually. In the majority of animals, even 20-30 minutes after cessation of rocking, complete restoration was not observed (Fig. 87). Full restoration was noted an hour after cessation of the rocking.

The influence on the organism of the animal of prolonged vestibular stimulation both by adequate (rotation) and by inadequate (calorization) stimulations interested investigators long ago, in particular those with the aim of localization of cortical projections of the vestibular analyzer.

Spiegel (1934) and Price and Spiegel (1937), in experiments /276
on cats showed that rotation elicited a general activation of EKOG diffusely in both hemispheres (especially in the ipsilateral one); these changes were more significant in the posterior portions of the supra- and ectosylvii gyri. Section of both fasciculi longitud med. at the level of the mid-brain or exterpation of the cerebellum did not eliminate changes in the electrical activity of the cortex with vestibular stimuli, i.e., vestibular impulses may reach the cortex of the cerebral hemisphere, passing both of these formations. Therefore the authors acknowledged that Held's vestibulo-reticular bundle participates in the transmission of vestibular impulses to the cortex.

Price and Spiegel (1937) emphasized that vestibular stimulation (rotation) elicits in an EKOG of curarized cats the same changes as with stimulation of other sensory nerves (suppression of slow waves, strengthening of swift oscillation). Moreover these changes are preserved even after removal of the cerebellum.

Gerebtzoff (1940) studied the influence of vestibular stimulation (rotation, calorization) to electrical activity of the cortex of the cerebral hemispheres of cats (preparation of encéphale isolé) in detail. The vestibular stimulation elicited a strengthening and increase in frequency of swift oscillations in the EKOG; but slow oscillations of alpha-waves were suppressed, i.e., according to

contemporary terminology, desynchronization of EKOG (activation reaction) began. Changes were noted in the entire cortex bilaterally but were maximum in the posterior corner of the supra-sylvii gyrus (Field 21 according to Broadman) primarily ipsilaterally. The threshold of reaction in this region was significantly lower. The given focus was activated even by rhythmic electrical stimulations of the 8th nerve. Cortical responses to vestibular stimuli disappeared after section of the lemniscus lateralis or of the peduncle of the inferior lamina bigeminum. Hence the author drew the conclusion that the anatomical path uniting the vestibular receptors to the cortex of the brain proceeds parallel to the central auditory path and forms relay stations in the inferior lamina bigeminum and the medial geniculate body.

Aspisov (1946) observed a general strengthening of electrical EEG activity with rotation of people. This strengthening was especially pronounced in the parietal region.

Zhirmunskaya and Ioselevich (1951) investigated in people the diffuse activation of EEG in response to calorization of the ear for the first 1 - 1.5 minutes. These changes were accompanied by vertigo. S. N. Khechinashrili (1958), polarizing the labyrinth with a bipolar current, elicited diffuse strengthening of electrical activity in both hemispheres on non-anesthetized preparations of encéphale isolé of a cat. Strengthening appeared especially strong /277 in the temporal and parietal lobes.

Gorgiladze and Fedorov (1964), also in experiments with polarization of the labyrinth of a cat with a steady current, observed the typical pattern of activation reaction, lasting throughout stimulation. With a low intensity of polarization (0.05 - 0.07 mA) the background activity was more noticeably changed in the regions of the supra- and ectosylvian gyri. Comparing the activating influence of various afferent stimuli (vestibular, pain, auditory, light), the authors showed that vestibular stimulation elicited a stronger effect of EKOG activation. With pharmacological exclusion of the reticular formation by aminazine, nembutal, or chlarolose, the reaction activation disappeared, which led the authors to conclude that the activating system of the reticular formation of the brain stem plays a leading role in electrographic reaction of waking in response to vestibular stimulation.

In the experiments of Aronov (1965) on human beings in darkness with closed eyes, accelerated rotation elicited depression in all groups of frequency components of the EEG's which he studied (7-8, 9-11, 12-20, 22-33 Hz), except for the group of 2-3 Hz, which did not essentially deviate from the background frequency.

In the light of contemporary concepts concerning the ascending activating system, each peripheral stimulus influences the cortex of the brain by two paths: through the specific paths and through the reticular formation of the brain stem. The influence through the specific path leads to the appearance in limited portions of

the cortex of electrical oscillations, whereupon these portions of the cortex sufficiently precisely correspond to the anatomical cortical projection of one analyzer or another. On the other hand, the given peripheral stimulation activates even the reticular formation of the brain stem through the collateral going from the specific path to the reticular formation. The reticular formation (its activating ascending portion) in turn influences the electrical activity of the cortex, not locally but more or less diffusely on both hemispheres. Thus each stimulus, including vestibular peripheral hemispheres by two paths: specific and nonspecific.

Insofar as the reticular formation receives constant impulsation both from vestibular receptors as well as from vestibular nuclei due to the presence of "labyrinth tonus" and close anatomical connections between the vestibular apparatus and the reticular formation, the exclusion of the vestibular afferentation must elicit a certain suppression of activity of the reticular formation, which in turn leads to a lowering of the tone of the brain. Actually, in the experiments of Kempinskiy and Ward (1950), stimulation of the motor cortex of a cat with threshold electrical stimulation after section of the 8th nerve elicited a noticeably weak motor activity of the extremity. Sometimes the activity was absent. Bilateral destruction of the labyrinth leads to a noticeable synchro- /278
nization of alpha-rhythm in the posterior sections of the cortex; in addition, the amplitude of potentials increases 2-3 times and sometimes 7 times (Gilman, 1963).

Diffuse changes in electrical activity of the cortex observed in our experiments with adequate stimulation of the vestibular apparatus and in the experiments of other authors (with rotation, calorization, or polarization) probably were elicited by activation of the reticular formation, and consequently such experiments cannot define the precise localization and the borders of the vestibular analyzer. Extensive incorporation of the reticular formation and reaction is explained by the prolonged nature of the applied stimuli and by the fact that the experiments we are considering were performed on non-anesthetized animals.

The close connection of the reticular formation with the so-called associative regions of the cortex probably explains the observations of many authors of the fact that the strongest changes of EKOG were in the posterior portions of the ecto- and suprasylvian gyri, adjacent to the associative regions.

The investigations we conducted on the bioelectrical activity of the cortex of the cerebral hemisphere and a number of subcortical formations, with stimulation of the otolith instrument by alternating linear accelerations, were limited to the study of summary bioelectrical potentials and were of a qualitative nature. Therefore, the results presented below, obtained in experiments with extracellular registration of activity of single neurons of the cortex and subcortical formations with consequent mathematical elaboration on a computer, are definitely interesting.

Change in the Activity of Single Neurons of Several Regions of the Cortex of the Cerebral Hemispheres and Subcortical Formations with the Action of Alternating Linear Accelerations[11]

With the aim of studying the localization of the central representative of the otolith receptor of the vestibular apparatus with the aid of electrophysiological methods, the regions of the brain of non-anesthetized curarized (with flaxedil) cats were investigated. Altogether 778 neurons were registered: 58 in the anterior sylvian gyrus, 74 in the auditory region of the cortex, 89 in the visual region of the cortex, 120 in the forward suprasylvian gyrus, 125 in the macrocellular reticular nuclei, 120 in the reticular formation of the pons, 87 in the black substance and 105 in the red nucleus.

Reactions of single neurons were investigated by vertical movement of the animals on a special stand. /279 Rocking took place periodically at a frequency of 15 - 20 rockings per minute and a maximum *G*-force of 0.8 to 1.2 *G*. Electrical responses of cells were removed with the aid of vitreous microelectrodes with a tip diameter of 1 - 5 μ. Responses, amplified by a UBP-1-01 instrument, were recorded on magnetic tape and 32 mm movie film. Experiments were conducted in a sound-and light-proof chamber.

The obtained results (frequency of impulses) were processed by two different methods. First the mean impulsation frequency was defined for equal periods of time and graphs of the changes in these frequenceis before, during and after rocking were made. Results of the analysis permitted dividing all neurons into the following 4 types.

Type I. Increase in impulsation frequency in comparison with the background. This type is subdivided into two groups: (A) increase of impulse activity to a maximum value comparatively swift (in the first second of rocking); (B) increase of impulse activity gradual. Maximum value of activity is attained in the 6th-12th second after the beginning of rocking.

Type II. Decrease in impulsation frequency. This type may also be subdivided into two groups: (A) decrease of impulse activity to maximum value after the first second of rocking; (B) gradual decrease in activity 8-14 minutes after the beginning of rocking.

Type III. Change in impulsation frequency has a phase character; i.e., in several seconds the increase in impulsation frequency during the period of rocking is replaced by a decrease; in several the opposite occurs.

Type IV. Absence of reaction to rocking.

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[11]This section was written with M. D. Venselum. Experiments were conducted by M. G. Kutaleladze and N. V. Merabishvili.

The presence of a large number of groups and types of neurons and also the absence of connection between the type of reaction and the region of the brain strongly hindered a solution of the assigned task.

As is known from the literature (Kastuk and Shapovalov, 1964) this impulsation frequency of neurons especially of those possessing spontaneous activity is a spatial, temporal summation of responses of a given cell to stimulation entering from the cells connected with it. Many afferent impulses coming from the cell are superimposed on its spontaneous activity, in connection with which the pattern of cell responses to stimulation becomes very complex. Evidently this explains the fact that the determination of the mean impulsation frequency for equal time intervals and subsequent construction of graphs according to these data did not give a univalued response to the question of which of the regions of the brain reacts specifically to rocking. In practically all regions, the change in the rhythmicity of neurons was approximately the same. This forced us to seek other methods of mathematical analysis, which would allow us to reply to the given questions.

The expediency of applying correlation analysis[12] for exposing /280 the nature of the reaction of an individual neuron to rocking is determined by the following circumstances.

(1) The distances between impulses of a neuron response are represented by random values (Petunin, Chorayan, 1966).

(2) Adequate stimulation changes according to periodic law.

(3) Single neurons of the brain regions conducted with the vestibular apparatus must react to rocking which manifests itself in a definite way on the correlation functions of their interimpulse intervals.

These premises provide a basis for expecting that investigating correlation functions of interimpulse intervals of the neurons of the brain region connected with the vestibular apparatus will show periodic components corresponding to the frequency of rocking. Finally, and in this case it is impossible to categorically assert the presence of a connection between these regions and the vestibular apparatus, it is possible to speak of their specific reaction to rocking.

As was noted above, electrical activity of the cells was registered on movie film. Deciphering the data, i.e., defining the duration of the interimpulse intervals, was conducted on an "Orbit"

[12]The use of this method relative to problems of a similar type of investigation was proposed and developed by M. D. Ventsel'.

instrument (Kalinovskiy, 1966) which allows one to plot the intervals on a perforated tape in a double code in the command system used for the "Dnieper" electronic digital computer.

In order to calculate the correlation function the following formula was used:

$$R_x(\tau) = \sum_{i=1}^{n-\tau} \frac{(x_i - M_x)\cdot(x_{i+\tau} - M_x)}{D_x\cdot(n-\tau)}, \qquad (1)$$

where $R_x(\tau)$ is the value of a normed correlation function with argument τ;

τ - 1, 2, 3,..., is the difference of the numbers in the series of interspike intervals;

x_i, $x_{i+\tau}$ is the value of the i-th interspike interval and the interval displaced in relation to it at τ intervals;

n is the total number of intervals;

M_x, D_x respectively, are the mathematical reliability and the dispersion of the sequency of interspike intervals. /281

The number of intervals fluctuated within the bounds of 400 - 700 as a function of their values. The frequency of the periodic components of the correlation functions was defined according to the original portions of the correlation function containing 200 - 300 points.

In connection with the fact that often the period of the correlation function is sufficiently difficult to define visually, in the cases necessary for approximation we used the least square method, considering that the normed correlation function is described by the expression

$$R_x(\tau) = Ae^{-\alpha\tau} + (1 - A)\cos\omega\tau, \qquad (2)$$

where the unknown parameters were α, A and ω. Analysis according to the least square method in each case could not be accomplished due to the fact that this required a great waste of machine time.

After the definition of parameters α, A and ω, the values of the approximated correlation functions for the comparison were plotted on a graph of an experimentally obtained function and then the number of points per cosinusoidal period were defined.

On the strength of randomness of the interspike interval values, the correlation functions constructed according to the ordinal number and directly according to time, generally speaking, were dif-

ferent. However, the values of the cosinusoidal period, defined by those and other methods correspond with a preciseness sufficient for application.

In several cases analysis according to time more clearly showed the periodic changes of correlation functions, but the process of manual deciphering makes this method practically useless. With a direct introduction of neuron responses into an electronic digital computer the method of analysis according to time becomes completely real. Evidently the best variance will be the parallel analysis of impulse activity of the cell according to the ordinal numbers of the interspike interval and according to time. Results of the application of this method of analysis to experimental data allowed us to divide all neurons into two groups; those reacting and those not reacting specifically to rocking. Those specifically reacting to rocking were considered to be those neurons whose impulsation frequency displayed a tendency to change periodically with the frequency of rocking. A typical correlation function of neurons not reacting specifically to rocking is shown in Figure 88. As is shown in the Figure, such a function is similar to the correlation function of a random Markov process and does not contain any visible periodicity. It can be approximated by the expression:

$$R_x(\tau) = Ae^{-\alpha\tau}. \qquad (3)$$

Neurons of such a type were registered in all investigated regions of the brain. An attempt to compare all correlation functions of this type along the parameter α did not yield clear differentation between different investigated regions. /282

Correlation functions of interspike intervals of neurons specifically reacting to rocking contained periodic components corresponding to the frequency of rocking. The form of this periodicity allowed us to separate neurons of this type into four groups.

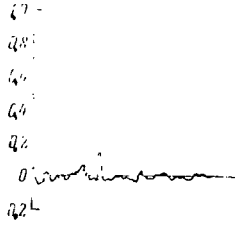

Fig. 88

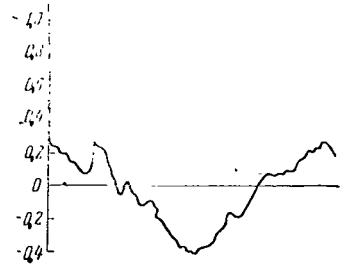

Fig. 89

Fig. 88. Correlation Function of a Neuron Not Reacting Specifically to Rocking (According to Ventzel').

Fig. 89. Correlation Functions of a Group A Neuron (According to Ventzel').

The correlation function of Group A neurons, the most numerous, may be approximately shown by (2). The typical example of such a function is shown in Figure 89. Evidently neurons of this group change in impulsation frequency in strict correspondence with the change in the value of the *G*-force. The impulsation frequency of the neuron constantly "follows" the change in the value and the direction of the *G*-force. To define the phase correlation between the frequency of rocking and the frequency of responses, i.e., with the aid of autocorrelation functions to determine which direction of rocking corresponds to an increase or decrease of frequency of neuron response, does not appear to be possible.

In the anterior suprasylvian gyrus, 70% of the neurons reacted specifically to a change in the value of acceleration (independently of whether the impulse activity increased or lowered in response to rocking). In all cases the period of oscillations of the correlation function coincided with the actual period of rocking (around 1.2 sec). In the remaining regions of the cortex, correlation curves of neuron activity did not contain a periodic component, and consequently reactions of the neurons in response to rocking were nonspecific.

Neurons of the remaining three groups were obtained only in /283 the reticular formation of the medulla oblongata.

The typical correlation function of Group B neurons is shown in Figure 90. Characteristic of a function of this type is the presence of separate surges at a distance of half the period of rocking from one another. Between surges the values of the correlation function are negative and do not exceed 0.1 - 1.3. Such a correlation function may correspond to a process in which groups (bundles) of impulses periodically arrive, which sharply differs from the whole sequence by the sizes of the intervals between them. It is possible to imagine that the bundles of impulses arise in such characteristic moments, recurrent with a period equal to half the period of rocking. It is logical to assume that these bundles arise

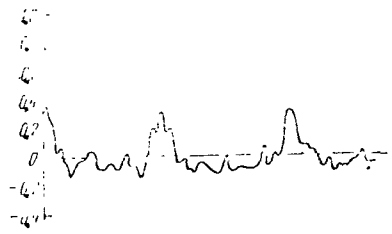

Fig. 90

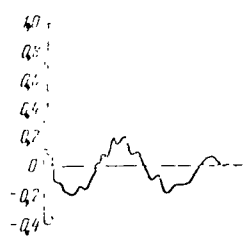

Fig. 91

Fig. 90. Correlation Function of Group B Neurons (According to Ventzel').

Fig. 91. Correlation Function of Group C Neurons (According to Ventzel').

at the moment when the rocking passes through the middle position, i.e., with a *G* force of 1 *G*. But it is possible also to imagine that a Group B neuron reacts with a change in its impulse activity only to a definite direction of *G*-force action, i.e., it generates bundles of impulses at the time of upward or downward rocking motion.

Group C neurons display in their correlation functions a clear periodicity of the frequency of rocking but, as opposed to group A neurons, their correlation function cannot be approximated by (2), since the point of the first intersection of the function with the axis of abscissa lies significantly closer to the beginning of the coordinate than 1/4 the cosinusoidal period (Fig. 91).

Among the neurons we investigated, a comparatively large number comprised Group D, the impulse activity of which presented a sequence of paired impulses (so-called doublets). As initial material for the calculation of the correlation functions of this type of neuron, the interimpulse distances both between doublets and within the doublets themselves were taken. Thus we introduce into the electronic digital computer a sequence of numbers which represent sequences of large and small intervals which were interrupted at the points where pulses of impulse activity of the neurons appear. The correlation function of such a sequence has unique character (Fig. 92). /284

In several cases the correlation functions seemed to represent pulsations, the junction points of which were removed from one another by approximately 1/2 the period of rocking. It is necessary to note that the impulse activity itself of neurons of this type is not strictly constant. Among doublets quite often one finds single or group (with more than 2 impulses) responses of cells, as a result of which the junction points on the correlation functions do not appear clearly pronounced. It is interesting to note that for all the investigated correlation functions of this type, an increase in the damping period of the higher frequency at the time of rocking, in comparison with the period before and after rocking, is characteristic. This indicates the more stable rhythmicity of the given

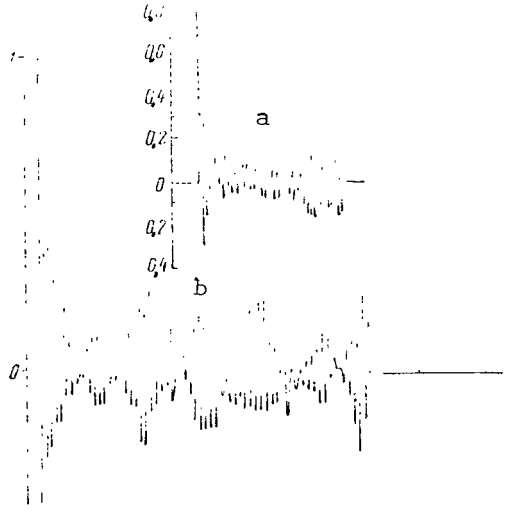

Fig. 92. Correlation Function of Group D Neurons (According to Ventzel'). (a,b) Before and During Rocking.

neuron, i.e., that the appearance of doubled impulses becomes more regular during rocking.

Types of correlations functions *c* and *d* are difficult to explain, although it is possible to imagine that they appear as combination of groups *a* and *b*.

It is necessary to note that the predominating type of reaction of the neurons of the brain stem was the activation reaction expressed in the noticeable increase in discharge frequency of the neurons during stimulation of the otolith organs. Moreover it was discovered that the number of neurons which are activated with rocking increases according to the conduction along the stem from the reticular formation of the medulla oblongata to the red nucleus /285
equal to, respectively 54, 63, 73 and 100%. The difference in the change in impulse activity of neurons in response to rocking in comparison with the background data (with a significance level of 0.05) was reliable in all cases.

The circumstance that practically all neurons of the red nucleus are activated by the action of acceleration evidently may be explained by the fact that the nucleus is responsible for the organization of muscle tone and posture. The vestibular stimulation reaching the red nucleus carries information demanding urgent mobilization and elevation of the activity of structures supporting tonic stress of the musculature and organizing new posture.

Extremely interesting, although still not properly explained, is the fact that according to the amount of conduction from the reticular formation of the medulla oblongata to the red nucleus, the number of neurons reacting specifically (by our definition) to rocking decreases surprisingly. Thus, in the macrocellular reticular nucleus of the medulla oblongata the number of specifically reacting neurons totalled 84.7%, in the reticular formation of the pons 54%, in the substance nigra 21%, and in the red nucleus only 6% (the remaining neurons reacted nonspecifically to rocking). Possibly this indicates the fact that under the conditions of the given experiments "the analysis" of entering information, basically, is performed in regions of the reticular formation, the neurons of which, as is known, possess developed collaterals ensuring them of wide-spread connections with the various structures of the brain.

As far as the black substance and the red nucleus are concerned, these formations basically form directing impulses for the organization of tonic stress and postural activity of the animal in response to the action of acceleration. Neurons located in the anterior ectosylvian, the medial-lateral and anterior suprasylvian gyri, in the majority of cases, responded to adequate stimulation of the otolith receptor with strengthening of the activity whereupon the number of "activating" neurons, respectively, equal 65, 60.7 and 70%. In addition, the changes in impulse activity of the neurons in response to rocking, in comparison with the background data (with a significant level of 0.05), were reliable in all cases.

Analysis of the obtained data by the method of correlation analysis showed that in the anterior suprasylvian gyrus, 70% of the neurons react to a change in the value of acceleration (independently, the impulse activity increases or lowers in response to rocking). It proved to be the case that correlation functions of interspike intervals in these neurons contain periodic components; in all cases the period of oscillations of correlation functions corresponded with the actual period of rocking.

Such correspondence indicates the fact that the neurons of the /286 anterior suprasylvian gyrus precisely react to a change in the value of acceleration; in other words, they specifically respond to stimulation. A periodic change in correlation function was absent in the visual (89 neurons) and auditory (74 neurons) regions of the cortex, as well as in the anterior ectosylvii (58 neurons) and in approximately 30% of the neurons of the anterior suprasylvian gyrus. Curves of correlation functions of these neurons proved to be typical for correlation functions of the random signal. Consequently a change in the value of interspike intervals was not connected with a change in the value of acceleration. We defined such a type of reaction as nonspecific.

Insofar as 30% of the neurons of the anterior suprasylvian gyrus did not display periodic changes of correlation functions, it is possible to assume that the vestibular apparatus (its otolith portion) is connected with this region by two paths: a short specific and a multisynaptic nonspecific path. The specific path passes, evidently, along the following formations: the vestibular receptors, the vestibular nerve, the vestibular nuclei, the thalamic specific nucleus and the anterior suprasylvian gyrus. The nonspecific path follows from the receptor to the reticular formation of the brain stem directly or across the vestibular nuclei to the nonspecific thalamic nucleus and hence again to the anterior suprasylvii gyrus. By means of this reticulo-thalamic system, evidently, a nonspecific reaction arises in two regions of the cortex. The first experiment of the application of correlation analysis for the investigation of reactions of various sections of the brain of cats to rocking permitted us to obtain several supplementary data characterizing the change in activity of the neurons of the investigated regions of the cortex and the brain stem in response to stimulation of the otolith apparatus. We succeeded in showing two characteristic types of reaction of neurons: tracing changes in the value of accelerations and separation of definite motions of the animals (possibly a change in direction) and to define region of the cortical representative of the vestibular apparatus (its otolith portion). The given region corresponded with that obtained in experiments with inadequate stimulation of the vestibular nerve. All this indicates the possible prospect for a method of solving several problems of physiology, in particular, definitions of the conducting paths of the vestibular analyzer (cf. also, Kutateladze, 1967a, b; Kutateladze, Merabishvili, Ventsel', 1967; Merabishvili, 1967).

Thus, vestibular stimulation of the cortex of the cerebral hemispheres, on the one hand elicits primary responses localized (in cats) in the anterior portions of the ecto- and suprasylvian gyri (if stimulation is discrete and short-term); on the other hand, it has a generalized diffuse activating influence on electrical activity of the cortex, which is expressed in a strengthening of the swift oscillations and suppression of the slow oscillation. /287 This is a typical picture of EEG arousal, which is observed with adequate and inadequate stimulations of other sense organs or with direct electrical stimulation of the reticular formation.

Convergence of Vestibular Afference of Signals and Afferent Signals of Other Origins on Cortical Neurons

One of the basic neurophysiclogical mechanisms of interaction of receptor systems, as was extablished by Fessar and his school (Fessar, 1962, 1964; Bynzer, Ember, 1964, et al.), is the convergence of afferent flows of various modality on the same structures of the brain.

The convergence of visual and vestibular influences on the cortical neurons of the primary visual projection zone (Field 17) of the cat were first discovered and investigated in Jøung's laboratory (Jøung, 1964).

An extensive investigation of the convergence of vestibular afferent signals and signals of other modalities on specific neurons in various cortical regions of the cerebral hemispheres, using a preparation of encéphale isolé of a cat, were conducted by Kornhuber and DaFonseca (1964). The authors registered the activity of neurons in g. g. ecto-suprasylvii anteriorae (primary vestibular region), in the medial and anterior regions of g. suprasylvius medialis, in the primary somatic region (g. postcruciatus), in g. lateralis anterior, in the primary auditory region (g. ectosylvius posterior), in the superior portion of g. ectosylvius posterior, in the rear portion of g. suprasylvius medialis, in Broadmans' regions 17 and 18, in the lateral geniculate body (sterotaxically through an intact brain and after suction removal of a brain tissue up to the lateral ventrical). A total of 474 neurons were registered. Reactions of neurons in the enumerated regions to visual (binocular diffuse white light, eyelids closed), vestibular (polarization, calorization) and acoustic (clicks, bangs, whistling, hissing) stimulation were investigated.

Responses of neurons to applied stimuli were divided into two main types by the authors: specific (Type I) and nonspecific (Type II). Specific responses were characterized by short and relatively constant latent periods, which began immediately from the maximum initial reaction (either activation or inhibition), strictly dependent upon the duration of the stimuli. For nonspecific responses, prolonged and variable latent periods were characteristic of a slow beginning of activation, which was prolonged and even sometimes in-

creased after the end of the action of the stimulus. Nonspecific responses depended on the condition of waking of the animals and arose to stimuli of various sensory modalities. The uniformity of nonspecific responses to stimuli of various modalities, a general appearance in the cortex and also the absence of precise temporal connections to the stimulus in them, contradict the hypothesis that such responses contain specific sensory information. It is difficult to imagine that cortical reactions with prolonged and variable latent periods continuing even after cessation of stimulation might be basic for precise sensory orientation. Responses of such a nature, on the other hand, are completely explainable by contemporary concepts on the role of the specific reticulo-thalamic system and the regulation of the level of waking and attention. /288

Specific responses to polarization of the labyrinth, even more numerous in g. g. ecto-suprasylvius anteriorae (the primary vestibular region), were rarely observed in the anterior and central portions of g. suprasylvius medialus or in the primary somatic and auditory regions, and extremely rarely in the visual and oculo-visual regions. The majority of specific responses in the vestibular regions had a latent period of 5 - 15 msec. The authors called such responses "primary specific responses", in contrast to the associative specific responses with more prolonged latent periods (25-150 msec). Neurons with specific associative responses more frequently reacted to stimuli of other modalities. With repeated stimulation, the reaction of such neurons (to auditory or visual stimulation) decreased or increased.

Using this criterion for the specific nature of responses of separate neurons assumed by the authors, most of the reactions of cortical neurons in Field 17 to polarization of the labyrinth, which Grüsser and coll. (1959) and Grüsser and Grüsser-Cornehls (1960) classified as indicators of specific vestibular influences and considered as a basis for the specific visual vestibular coordination, it would follow to classify them as nonspecific. Grüsser and Grüsser-Cornehls (1959) based their assumption on a number of generally known psychophysiological observations. But these observations may be explained even without admitting the specific vestibulo-visual coordination. Thus, it is known that vestibular stimulations (rotation or galvanization) in man elicit a disturbance not only of the visual but also of the auditory and tactile sensations (Bechterev, 1896).

Kornhuber and DaFonseca separated 6 subtypes of specific reactions of the cortical neurons to polarization of the labyrinth. The reactions of three subtypes depended upon the direction of polarizing current, while three did not depend on the direction of polarization current. Two-thirds of specific responses registered in the vestibular cortex belonged to the neuron group whose reactions depended upon the direction of a low-intensity polarizing current (0.5 - 2 mA).

In the majority of cases, subtypes of specific reactions did /289

not remain constant with an increase in intensity of the stimulus, but were transformed into one another, which the authors connect with the convergence of afferent signals from various vestibular receptors of one labyrinth. Actually, as Duensing and Shaefer (1959) showed, for a majority of neurons of vestibular nuclei the convergence of impulses is characteristic even from the semicircular canals and from the macula. Moreover, vestibular afferents, converging on the cortical neurons, differ in threshold and character of reaction. Thus Anderson and Gernandt (1954), as was noted above, discovered various cortical projections of separate vestibular organs which, at the same time, had insignificant regions of intersection.

Insofar as in experiments no difference between responses of neurons of the vestibular region were found which depended on the direction of polarizing current to the ipsi- and contralateral stimulation, Kornhuber and DaFonseca assume that both hemispheres under natural conditions, receive equal information on the direction of acceleration, i.e., that the vestibular cortical projection is bilateral. Such a reaction is characteristic for neurons reacting to vestibular stimuli of the reticular formation of the brain stem, but is not observed in neurons of the vestibular nuclei (cf. Chap. III). Probably the reaction of neurons of the vestibular cortex is explained by the functional intersection of vestibulo-reticulo-thalamic projections. Insofar as barbiturate anaesthesia substantially suppressed ipsilateral responses, the authors assume that intersecting paths are basically monosynaptic, while ipsilateral paths have several synapses in the reticular formation. Such a conclusion is strengthened even more by the data from experiments on monkeys (Fredrickson et al., 1966).

The rhythm of neurons of the vestibular cortex did not correlate with nystagmus arising with polarization of the labyrinth, but if the eyes of the animal were open, discharges of neurons were grouped in the rhythm of nystagmus. Duensing and Shaefer (1958) showed that with closed eyes, in many neurons of the vestibular nuclei correlation of change in the discharge frequency with the rhythm of nystagmus is observed. Consequently the results of Kornhuber and DaFonseca are explained either by the fact that the neurons of the vestibular nuclei projecting to this element do not have nystagmus modulation, or such modulation exists but it is removed in the thalamus. The assumption that nystagmic rhythm (the swift phase of nystagmus) is coordinated not in the vestibular nuclei but in the reticular formation agrees with the conclusions of Lorente de No (1933b) and Duensing and Shaefer (1957, 1958). In this case frequency modulation of neurons of the vestibular nuclei in the rhythm of nystagmus would be elicited by recurrent reticular connections (Lorente de No, 1933b).

The authors assume that the rhythm of nystagmus defined by /290
the swift phases, is an automatic process accomplished in the brain stem which is corrected only by the cortex of the brain. The fact that the grouping discharges of neurons of the vestibular cortex in

the nystagmus rhythm takes place only with open eyes attests to the fact that information not about swift phases of nystagmus as such, but about the result of eye movements (the appearance of new objects in the field of vision after swift deviation of the eyes) enters the cortex.

Nonspecific reactions of neurons to polarization of the labyrinth, in the experiments of Kornhuber and DaFonseca, were registered in all investigated regions of the cortex, even in the lateral geniculate body with sterotaxic registration through the intact hemisphere. These reactions were manifested in the form of activation; inhibition of activity was noted only in the anterior portion of g. lateralis.

G. I. Gorgiladze and G. D. Smirnov (1967), investigating the influence of the vestibular stimulation on neuron activity of the visual cortex of the cerebrum in a cat, likewise did not observe a single case of suppression of neuron activity in the primary visual projection zone in response to polarization of the labyrinth.

Specific reactions of the cortical neurons to visual stimuli were discovered by Kornhuber and DaFonseca in Broadman's regions 17 and 18, in g. suprasylvius medialis, g. ectosylvius posterior, and also in the vestibular cortex (which actually had a more prolonged latent period). In the primary somatic region, responses to light were infrequent and variable.

Two-thirds of the neurons of the primary auditory zone reacted specifically to auditory stimuli, while in the vestibular regions only 1/3 of all neurons so reacted. Irregular specific auditory reactions were noted in the primary somatic region, the visual region g. lateralis anterior, and g. suprasylvius medialis.

Convergence of specific responses to stimuli of one modality and nonspecific responses to stimuli of other modalities were discovered by Kornhuber and DaFonseca in all regions of the cortex and in the geniculate body.

The greater portions of neurons of the auditory, visual and oculo-visual regions, (including g. suprasylvius and g. ectosylvius posterior) show convergence of auditory or visual responses and nonspecific responses of another origin.

For nonspecific activation, the intermodal interaction proved to be principally the same for all afferents. Specific excitation was strengthened nonspecifically until maximum response was reached. For this reason, specific primary activation usually either did not arise or arose insignificantly. Specific inhibition always sominated nonspecific excitation. Therefore types of specific activation remained constant during nonspecific influences. Thus, in the experiments of Gorgiladze and Smirnov (1967), polarization of the labyrinth, together with strengthening of impulse activity of the neurons of the visual cortex, stabilized and strengthened the reaction /291

of activation, to a light burst, characteristic for the given neuron. If the neurons reacted weakly to light, or its reaction was unstable, then with polarization of the labyrinth the same stimulus clearly shows that this neuron belonged to one or the other type. Precisely such changes in reactions of neurons to the light were elicited even by pain stimulation of the skin. It is important to note that Gorgiladze and Smirnov did not even once observe disappearance of the reaction of neurons to light stimulus with sharply expressed strengthening of impulse activity in response to polarization of the labyrinth or to cutaneous pain stimulus. The fact that the influence of the vestibular stimulation on the primary projection of the visual zone is not specific, i.e., not connected with information input into the cortex characteristic for the given systems of receptors, is supported even by the similarity in the changes in neuron activity observed under these conditions in various regions of the cortex of the cerebrum.

There is convergence of specific afferents of various modalities on the same neuron. In the experiments of Kornhuber and DaFonseca, this was rarely observed. For example, specific optico-vestibular convergence was discovered only in neurons of the vestibular region, partially encompassing the second somato-sensory region (not considered one of the neurons of the visual cortex). Such visual vestibular neurons also reacted to sound, i.e., they were at very least trisensory. Vestibular responses of these neurons depended on the direction of the polarizing current and were distinguished by low spontaneous activity, which is possibly a characteristic of neurons with specific convergence, since the only trisensory neurons of the visual region also possessed low spontaneous activity.

Bisensory specific acousto-vestibular convergence was discovered chiefly in the vestibular region, and more rarely was found in the primary somatic region in which neurons with acoustical visual convergence were occasionally observed.

Mickle and Ades (1952), applying the method of elicited responses, showed that the vestibular cortex is a multisensory region with broad convergence of vestibular, somatic and auditory afferents, which probably is important for maintaining posture and spatial orientation of the animal. On a preparation of *encéphale isolé*, Kornhuber and DaFonseca (1964) were not able to investigate convergence of somatic afferents; but Berman (1961), studying the secondary somatic region of the cortex of the cat, discovered that pulvinars of the anterior and posterior extremities are projected in the vestibular region. /292

Fredrickson et al. (1966), in experiments on monkeys, showed that in the vestibular cortex there is a region 5 x 3 mm in size where responses to stimulation of the medial nerve of the anterior extremity are registered. All these facts support the hypothesis that integration of afferents bearing information on posture takes place in the vestibular cortex.

Specific convergence is basic for integration of visual, auditory, vestibular and somatic afferentation. It is necessary to note that localization of the region of convergence in the cat agrees with the data on man, in which destruction of perception and visual postural coordination is observed after injury to the frontal or parietal but not the occipital region of the cortex (Kornhuber, DeFonseca, 1964).

Electrophysiological experiments which have been performed to data show that the so-called specific cortical convergence of visual, vestibular, auditory and also, in all probability, somatic afferentation takes place almost exclusively in the anterior portions of the ecto- and suprasylvian gyri; i.e., in the portions of the cortex defined as cortical projection fields of the vestibular analyzer. Therefore the assumption of Gorgiladze and Smirnov (1967), which states that the "vestibular cortical field is the coordination center which integrates afferent impulses from various sense organs and creates images of spatial relationships between the individual and surrounding objects of the visible world", appears to be correct.

CHAPTER X

CORRELATIONAL STEREOTAXIC RELATIONS BETWEEN VARIOUS ORIENTATION SYSTEMS IN THE HUMAN HEAD[13]

In the preceding chapters, the different aspects of the mor- /293
phology and function of the vestibular analyzer were considered in detail. With the presentation of the material, especially with the description of the most precise spatial architectonics of the morphological structures of the labyrinth, attention was directed to the circumstance that the description was not accompanied by an explication of the general correlation connections of these structures with the skull and the orientation systems of the head. Meanwhile, even the most precise differentiation of morphological structures of the peripheral receptors of orientation and the specific nature of their functional designations must not lessen the significance of the fact that all these structures are not only united morphologically with the structure of the skull, but also functionally, since they all serve, in the final analysis, the accomplishment of one goal: the optimal realization of the process of orientation of the animal in three dimensional space.

The Head of Man and the Higher Vertebrate Animals as the Bearer of Basis Orientation Systems

Comparing the significance of the separate peripheral receptors of orientation with each other, i.e., the number and content of orientation information sent by them into the central nervous system, it is impossible not to note that the fundamental ones (visual, labyrinthal, acoustic, olfactory and partially cutaneous) are concentrated within the confines of the head.

Such a regularity does not appear to be accidental if we /294
consider that the receptors of orientation basically are excited and function in the process of completion of movements, including various changes of position in space. In man, and particularly in animals, a significant number of completed movements are performed to accomplish spatial orientation, and in turn spatial orientation is performed for the most part, to accomplish movement. In other words, motion serves as the initial and final link in a process of collection, analysis and use of orientational information. In

[13]This chapter was written by B.P.Simchenko, S.I.Khmelevskiy and [B.T. Chernykh

general, it is often impossible to separate movements which are completed with the goal of gathering orientational information for movements which are only the consequence of the analysis, and the actual use of the data of this information. As a result of such a process, the constant correction of spatial orientation behavior of a man or of an animal takes place.

Unity, or the functional fusing of kinematic characteristics of the mechanism of vestibular reaction with reactions of other peripheral receptors of orientation and also with reactions of the motor systems, orienting and stabilizing the body in space necessarily leads to the consideration of the expediency of investigating the adequate unity of morphological structures of these systems in the sense of their stereotaxic, correlational interrelationships.

If the spatial behavior of higher vertebrate animals and man is viewed from this position, it is possible, in addition, to note that with head motions the same regularities are manifested to a greater degree than with movements of the trunk.

This takes place according to the following two principles. In the first place, the head of man and of all higher vertebrate animals (except for fish), due to its cervical-spinal section, possesses relative independence of motion. In the second place, the head serves as the bearer of the majority of basic peripheral receptors of orientation.

In the nerve mechanisms of reactions of the peripheral orientation systems, as well as in the nerve mechanisms of motor systems orienting and stabilizing the body in space, both of these principles are essential in logical and functional relations. The first of these emerges as a constructive mechanical condition for the capacity for elevated mobility of the head in comparison with the trunk; the second as a dynamic necessity for the existence of elevated mobility. The gathering of visual, auditory and olfactory information, generally speaking, may be connected with the necessity of "tuning" a given peripheral receptor in the direction for the appearance of a maximal signal, either in strength or in its significant content. All these head motions, taken together, /295
may be accomplished both simultaneously with the body, which is less expedient and is not even always possible, as well as in relation to the body, which is more expedient and effective. And naturally this brings close attention to the system of the occipito-atlantal and atlanto-epistrophic articulations, especially in connection with the appearance of possible antidromic correlation connections of various orientation systems concentrated within the head, i.e., in the system of these articulations.

The legitimacy of such an investigation will become especially evident if we raise the question of the functional significance of these articulation systems. Certainly, due to them supplementary

facilities are created for the taking of nourishment and for attack and defense. However, it is necessary to reply to this question in the following way.

The system of occipito-atlantal and atlanto-epistrophic articulations in higher vertebrate animals and man serves chiefly to create optimal conditions for the gathering of various types of orientational information: visual, labyrinthal, auditory, gustatory and thermal, proceeding to the head of the man or animal from various points of space.

The Conception of the Anatomo-Physiological Center of the Skull in the Central Nervous System of Man

Even a simple, brief glance at the mutual distribution and orientation within the human skull of separate elements of the labyrinth and of condyles on the occipital bone indicates that between them there are close correlational stereotaxic interrelations.

Actually, the centers of both labyrinths (their utricular regions) lie in the same frontal plane of the skull *YOZ* (cf. Figs. 93 and 94) as the centers of operative surfaces of condyles connected with the atlas. The center of symmetry of both labyrinths (point *O*) is removed from them at the same distance as from the working surfaces of the condyles, on the average equal to 40 mm (from measurements on a series of 38 skulls).

Observations of similar nature and also considerations presented in the preceding section directed our attention to the investigation of the system of the occipito-atlantal and atlanto-epistrophic articulations in man.

For this a special instrument, "a chorograph", was applied, which permitted us to conduct volumetric anthropometric measurements of combined surfaces in the system of these articulations. The method of measuring included preliminarily obtaining plaster models by taking molds with specific elements of articulations (condyles, atlas, epistropheus and its teeth), which allowed us to facilitate the work of measuring and increase its precision.

The following was established. The curvature of the joint surfaces of the atlas (and the condyles) in the sagittal and frontal planes was different: in the first, the radius of curvature on the average was equal to 30 mm, and in the second, 50 mm.

Centers of curvature of these surfaces lie on the straight line *JOZ* (Figs. 94 and 95). If we continue the straight line downward (to the point *G* and below) then it will pass as the axis of symmetry through these links of occeus tissue of the cervical vertebrae, which in the vertebral column work against deformation

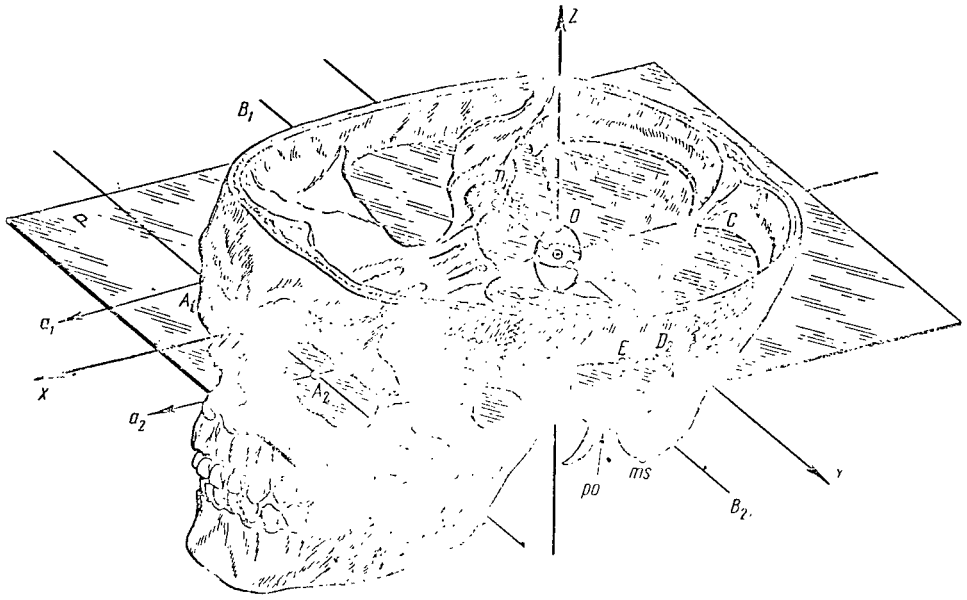

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Fig. 93. The Spatial Localization in the Human Skull of the Anatomo-Physiological Center Region and the Position of the Horizontal Physiological Plane (According to Simchenko, Khmelevskiy and Chernykh) A_1 A_2: Pupil Line; A_1a_1 A_2a_2: Rays of Vision of the Left and Right Eye; B_1B_2: Interaural Line: $XOYZ$: Three-Dimensional Spatial Reference System with the Center in the Region of the Anatomo-Physiological Center; C: Point of Intersection of the OX Axis with the Internal and External Surface of the Skull; D_1D_2: Points of Intersection of OY with the Internal and External Surface of the Skull; *po* (porion): Point on the Middle of the Upper Edge of the External Acoustic Meatus; *ms*: Point on the Lower Edge of the Mastoid Process; Dotted Line: the Lines of Intersection of the Horizontal Physiological Plane with the External and Internal Surface of the Skull and Also with the Region of the Anatomo-Physiological Center (0).

of compression; i.e., they counter gravitational forces of the head. (Starting from these considerations, the straight line $GJOZ$ henceforth will be considered as the vertical axis of the cervical region of the spine and of the human skull as a whole).

The centers of gravity of the contact areas of the atlas and the condyles are distributed on straight line 7 which lies in the frontal plane YOZ and therefore intersects with the vertical axis of the skull $GJOZ$ (at point J in Figs. 94, 95 and 96). Given direct lines uniting the joined contact areas on the atlas and epistropheus (line of juncture of these areas is No. 4, Fig. 94) are subordinate

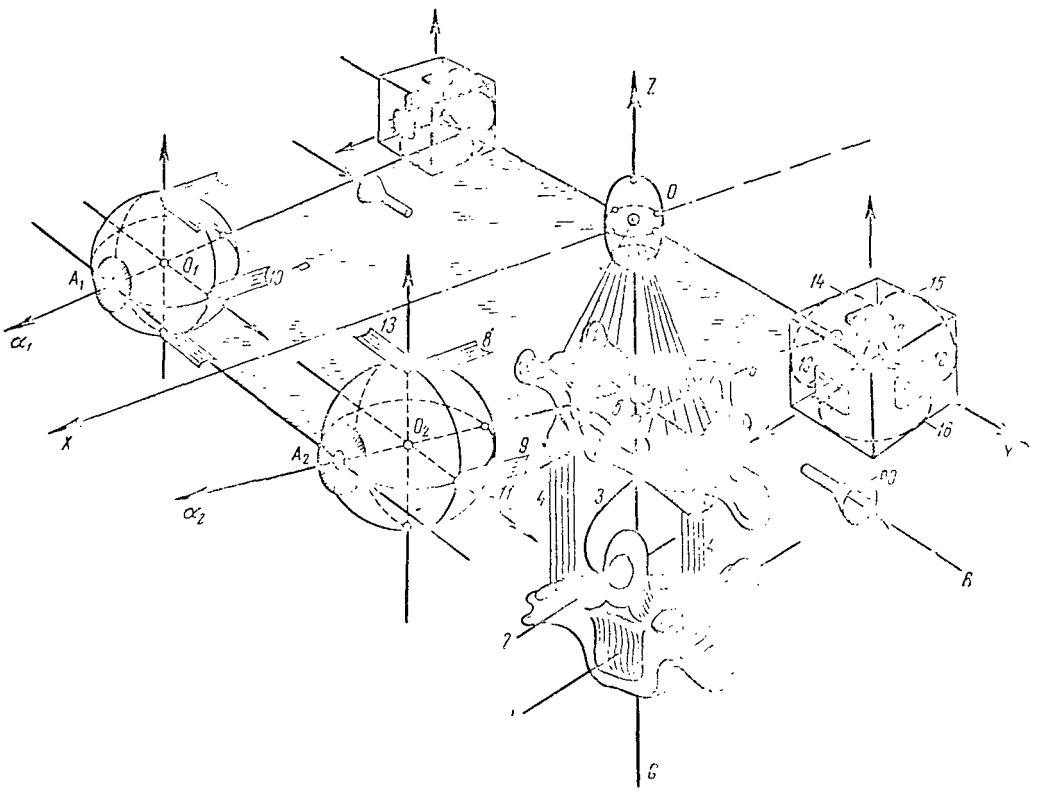

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Fig. 94. Kinematic and Constructive Subordination of a Sixth Polar System of the Vestibular Apparatus and Oculomotor Muscles to the Structure of the Anatomo-Physiological Center in the Kinematic System of the Atlanto-Epistrophic Articulation (According to Simchenko, Khmelevskiy and Chernykh). (*B*) Direction of Reception of Maximum Auditory Information; (1) Longitudinal Sagittal Axis of the Second Cervical Vertebra (Epistropheus); (2) Horizontal Longitudinal Axis of the Contact Area the Tooth of the Epistropheus with the Corresponding Operative Surface of the Atlas; (3) Arrow Indicating the Conjuncture of a Tooth of the Epistropheus with the Atlas; (4) Lines Indicating the union of the Corresponding Articulated Surfaces of the Atlas and the Epistropheus; (5) Radius of Curvature (with the Center in Point *L*) of Articulated Surface of the Atlas Area Contacting with the Tooth of the Epistropheus); (6) Longitudinal Sagittal Axis of the Atlas; (7) Tranverse Axis of the Atlas of Passing at the Level of the Center of the Contact Area of the Atlas with the Condyles of the Occipital Bone of Skull (*J*); (8-13) Respectively: Superior, External, Internal, Inferior, and Oblique Eye Muscles; (14) The Anterior Vertical Canal; (15) Posterior Vertical Canal; (16) The Horizontal Canal; (17, 18, 19) Membranes and Neuroepithelium,

Respectively, of the Utriculus, sacculus, and its subdivision - the sacculusseca; *OG*: axis of horizontal rotations of the head in the plane *P*; O_1,O_2; optic centers of the eyes. Remaining designations the same as in Fig. 93. /298

to this law, and also on the epistropheus and the third cervical vertebra etc. Finally, the curvature of the joined surfaces of the tooth epistrophy and the corresponding surface of the atlas have, on the average, a radius equal to 5 mm, due to which the center of curvature of surfaces *L* (Figs. 94, 95 and 96) also lies in the vertical axis *OZ*.

We will not describe the results of the measurements in greater detail, but we shall formulate the conclusions which proceed from them.

The systems of the occipito-atlantal and atlanto-epistrophic articulations, from the kinematic point of view, represent a three-dimensional unitary spatial articulation with three degrees of freedom.

In the system of these articulations there is a constructive division of functions. The occipito-atlantal articulation is a system of paired, symmetrical, firmly connected articulations determining rotational movements of the head in the sagittal plane around the axis *OY* (deflections of the head forward and backward) and on the frontal plane around the axis *OX* (deflections of the head to the left and the right). The atlanto-epistrophic articulation determines chiefly rotation of the head in the horizontal plane *P* around axis *OZ*.

With rotation of the head around the axis *OX*, the center of rotation, i.e. the point of maximum rest, is at a distance of $\approx$ 50 mm with rotation around the axis at a distance of $\approx$ 30 mm from the condyles; with rotation around axis *OZ* on the vertical axis *GOZ* uniting the two preceding centers. If the head completes free rotational motions in various planes, then a summation of the described simple components of the rotational movement takes place which, taking into account several displacements on the level of the third, the fourth, etc., vertebrae, gives the total number of possible locations of instantaneous centers of rotation in the shape of an ellipsoid, the larger axis of which corresponds in space with the vertical axis of the skull *OZ*. The center of this region (point *O*) may be isolated as the point of maximum rest in an intrinsic relationship. This is the same point which serves as a geometrical center of symmetry of both labyrinths and is at a distance as is noted, of $\approx$40 mm from the condyles and the labyrinths themselves. /299

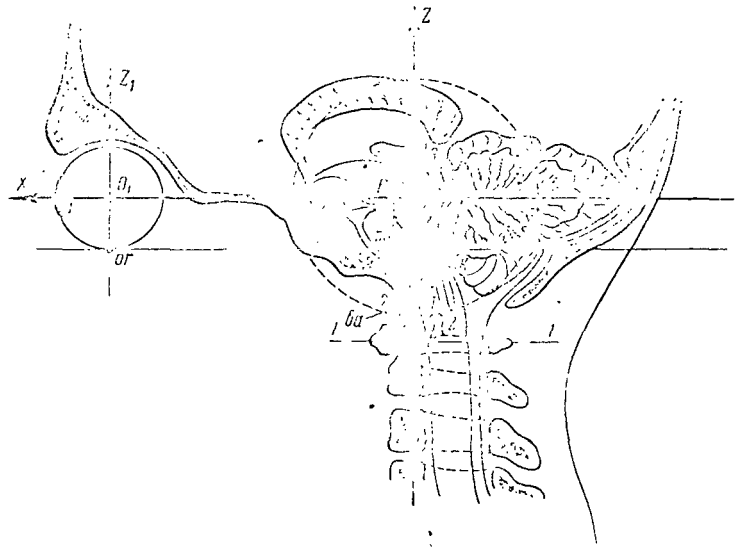

Fig. 95. Stereotaxic Localization of the Region of the Anatomo-Physiological Center Among Various Sections of the Brain in Sagittal Section (According to Simchenko, Khmelevskiy and Chernykh). XO_1Z_1: Three-Dimensional Reference System of Head and Orbit Motion: (1-1) Horizontal Sagittal Axis of the Atlas; (2-2) Contour of the Contact Area of the Atlas; (3) Lamina Quadrigemina (4) Fourth Ventricle; *ba*: basion (Point on the Interior Edge of the Occipital Opening); *or*: Orion (Inferior Point on the Orbit of the Eye); Dash-Dot Line *po-ms-k*: Projection the Contour of the Ear Opening of the Skull and the Mastoid Process on the Sagittal Plane of the Skull. The Maib Designations are the Same as in Figures 93 and 94. /300

Thus, with "relative" rotational motion of the human head in arbitrary planes in relation to the trunk, both labyrinths perform absolutely symmetrical oscillation, i.e., equal in trajectories and amplitudes, but different in size (excluding the case of pure rotation around the axis *OY*) whereupon the intrinsic center of these oscillations is point *O*. This point serves simultaneously as a constructive (anatomical) and kinematic (physiological) center of the system of the three-dimensional joint articulation, with the aid of which the human head is affixed to the vertebral column. Thus it proves to be the center of intersection in space of the axes *ox*, *oy*, *oz* with the rotation of the head in the three spatial coordinate planes.

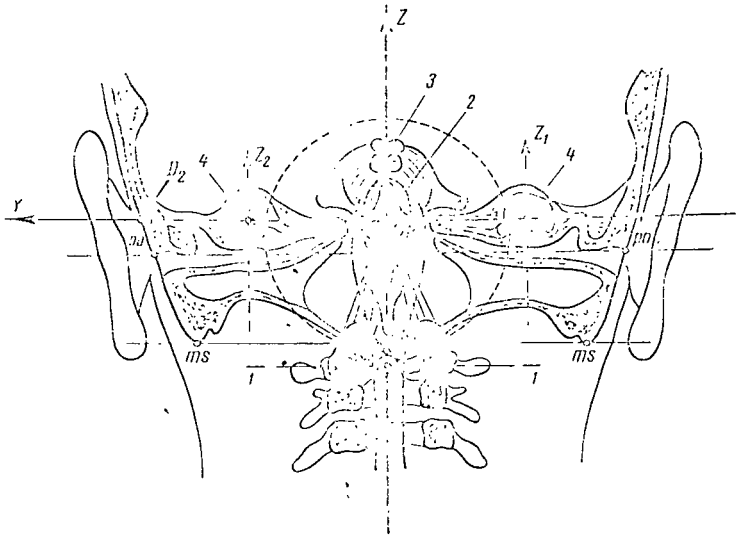

Fig. 96. Stereotaxic Localization on the Region of the Anatomo-Physiological Center Between Various Sections for the Brain and the Frontal Section (According to Simchenko, Khmelevskiy and Dhernykh). (2) Fourth Ventricle; (3) Lamina Quadrigemina; (4) Ventricular Apparatus. Remaining Designations the Same as in Figures 93 and 94.

The latter conclusion is fundamental for the conception being /301 expounded. On the basis of this we will further define the ellipsoidal region with the center at point *O* (see Figs. 93, 94, 95 and 96) as a certain stato-kinematic center (the human skull; systems of the left and right vestibular apparatus) and also systems of spatial articulation (the condyles-atlas-epistrotropheus, which, for the sake of brevity, we shall indicate as CAE).

We shall consider voluntary head movements, and consequently all their orientational systems, as complex ones which consist of two simple components: transferable motion together with the body and relative motion on the body. Such reasoning has only a purely symbolic sense for our object of investigation, but has a very concrete functional content. The fact is that with spatial motions of the animal and with control over these motions, for the central nervous system, it is extremely important to distinguish signals coming from the peripheral receptors of orientation and indicating a change in the coordinates of the body among the surrounding objects in space and signals coming from those same receptors but giving information on the change of directional position of the body in relation to these objects.

This reckoning is important in general, but especially because the majority of orientational signals originate from the peripheral receptors of the head, caused by independent movements in relation to the body.

For the differentiation of these signals in the central nervous system, evidently the CAE plays the decisive role. Due to the extremely high correlation coefficient which exists in the stereotaxic

relationships between the labyrinth and the constructive parameters of the kinematic system of this articulation (the range of variations of anthropometric criteria of the connection between them is very small), differentiation of signals takes place even during the very first stage of this analysis, i.e., at the input to the system. It must be assumed that the principle of differentiation consists of the following: if signals from both labyrinths were elicited by absolutely equal amplitudes (in the sense explained above) their motions around the CAE the summary signal, going to the following stage of analysis of orientational information, "speaks" to the fact that relative motion is taking place, i.e. a change in directional position; if, however, these signals have different amplitudes, then this testifies to a transferable motion, i.e. of a change in spatial coordinates.

We have said above that the CAE region and its nucleus (point *O*) serve within the skull as the zone of greatest dynamic rest. This circumstance forced us to direct our attention to the specifics of localization of various sections of the brain and spinal cord in man in relation to the CAE region. /302

The regular development of the given investigation in this direction becomes very apparent if we consider that between the transferable and relative head motions there are not only functional-orientational, but also purely quantitative, differences. The point is that the usual relative motions of the head elicit, in various regions of the brain, inertial effects which are several times greater than the usual transferable motions of the head together with the body.

We will compare, for example, the following two motions: rotation of the head on the body at 180° for 0.25 sec, and banking on a motorcycle with a banking radius R_2 = 10 m corresponding to this rotation in centrifugal effect.

For centrifugal force in the first and second case we will have

$$F_1 = m \cdot \frac{v_1^2}{R_1} \text{ and } F_2 = m \cdot \frac{v_2^2}{R_2}.$$

Comparing these forces we obtain the following dependency:

$$\frac{v_2}{v_1} = \sqrt{\frac{R_2}{R_1}}.$$

From the last expression it follows that if the radius of rotation is increased, for example, by 100 times, then the linear velocity of this rotational movement will increase by 10 times. In our case linear velocity of the frontal lobes will be v_1=120 cm/sec.

Insofar as the linear velocity of the motorcyclist must be ten times greater, then this sets the value at 12 msec, which corresponds to banking at a speed of 46 km/hour with a radius of banking of 10 m. It is clear that such transferable motions are rarely found in life.

Thus, in the usual life of a man and even more in the lives of animals whose heads, as a rule, differ by their greater mobility, transferable motions of the head cannot in any way be compared with relative motions. Therefore, if in the evolutionary development of animals the problem of preservation of the smallest and most important structures of the brain and the spinal cord have arisen from various inertial effects of head movements, then it is clear that the role of these zones in the skull cavity, which border with regions of its CAE, and even more of the role of the CAE nucleus itself, will increase even more.

The investigation of the specific characteristics of the localizations of various sections of the brain and the spinal cord /303 within the human skull indicate that in the CAE region were located: the fundus of the fourth ventricle-rhomboid fossa with the nuclei of all the craniocerebral nerves, with the exception of n. opticus and n. olphactorius; the subcortical nuclei (centers) of cardiac activity and of respiration; the vestibular nuclei and the motor nuclei of the systems orienting the body; the subcortical nuclei of the auditory and visual analyzers (near the upper border of the CAE region; see Figs. 95 and 96); the pineal gland; the peduncles of the cerebellum, originating from the CAE region, as from the center; the aperture of Lyuska and the central aperture of Magendie; finally the reticular substance which fills a significant portion of the volume of this region.

If we speak about the nucleus of the CAE region itself (point *0*), then it is localized at the fundus of the fourth ventricle, i.e. through a fluid secreted by the first, second and third ventricles, and first enters in the region of the CAE of the skull, and then from it, as from the center, it is distributed above all the subarachnoidal space of the brain.

Considering these circumstances and also the entire complex of concepts and conclusions of the present investigation, the authors considered it expedient to define the region defined above as CAE as a special region of the skull, the head and the central nervous system of man in a stereotaxic, kinemactic, automatic, and physiological sense, and to call it the anatomo-physiological center (APC) of the skull, the head and the central nervous system of man.

Here we note that the conception of the APC of the human (and animal) head and central nervous system does not have anything in common with the known theory of Pennfield and Jasper about the so-called "centricephalic system" of the human head, according to which the reticular formation is the bearer of consciousness,

although the basic mass of reticular substance is concentrated in the APC region.

The basic means of the proposed concept consists primarily in the fact that it will evidently be able to play a definite role in anthropology, biology and medicine, permitting one to unite various information and regularities of these regions, such as: architectonics of the cerebral section and their conditioned reflex connections, blood and fluid dynamics and neurosurgery, myology of the mandibular and cervical articulations and also the mechanism for joining of their motions; the method of compilation of stereotaxic charts and plans of the brain and the construction of stereotaxic instruments; morphology and physiology of the labyrinth and octolaryngology; general questions of onto-and philogenesis of the animal world in connection with ideas about the APC of the head.

Preconception of Anatomo-Physiological Center of Man in the Phylo- and Ontogenetic Aspect /304

The region of the future APC in the adult man serves in the embryo, in the very first stage of its development, as the point of origin of the growth and formation of the central nervous system. It is known that in the embryogenesis of the fourth ventricle and its fundus, i.e., the rhomboid fossa (that is, only the structures in the volume of the APC which would represent its nucleus), are formed as the first regions of the brain and spinal cord. It is curious that the establishment of the rhomboid fossa is apparent even in the case when an acephalic fetus is born.

Concepts of a similar nature are basic for the development of the concept of the APC in the areas of embryogenesis and obstetrics (Malinovskiy et al., 1968).

Investigations in this direction were conducted with the participation and under the guidance of M.S. Malinovskiy and B.V. Ogneva.

The APC region, from the first stage of embryological development and also in an adult human being, is located in the place in the organism which serves as the single point of culmination in pairs of all three different types of symmetry: the central (the APC nucleus serves as a physiological and partly anatomical center of symmetry of the brain, its cortex and subcortex); axial (the axis of symmetry of the spinal cord and the Medulla oblongata passes through the APC nucleus); and bilateral (sagittal plane of symmetry of the left and right portions of the central nervous system also passes through the APC nucleus). In addition, all these types of symmetry were characteristic for the remote phylogenetic predecessors of man, i.e., at first separately, then parallelly and finally united. This provides supplementary delimination to the question of morphological investigations of architectonics of various sections of the central nervous system as a whole, and its peripheral

receptor orientation in particular.

The fact of the matter is that the localization of most important sections of the central nervous system (in relation to life) in the APC region is an expression of the optimal structure and function of the central nervous system, not only in the sense of dynamic preservation of its basic modular sections, but also in the fact that located here they have a more expedient system of connections with all the other sections of the central nervous system.

According to the reflex theory of stimulation of growth of brain cells (Klosovskiy, 1947, 1954), the decisive influence on their formation and growth is shown by nerve impulses proceeding from the peripheral receptors beginning to function at this time. In addition, the authors give particular significance among/305 these regions to the labyrinth: in the first place, because motions are the source of its stimuli, which the fetus always possesses in abundance, both in the form of relative rotations on the umbilical cord as well as in the form of transferable rotations with the body of the pregnant woman; and in the second place, because orientational information of the labyrinth, determined by gravitational and inertial actions, serves as the only source of information for the central nervous system on the characteristics of the three-dimensional space in which it is forming.

With the development of investigations in this direction it was discovered that the head of the fetus and the newborn infant possesses indications testifying to the existence of its own APC. Moreover, the origin and formation of the labyrinth and also myelinization of the fibers innervating it, which are stimulated by nerve impulses, greatly surpass the same processes in other receptors. It is all the more significant that the labyrinth serves as one of the basic elements entering into the concept of APC, and therefore the mechanisms of formation of the labyrinth are very significant.

In connection with this, it is expedient to separate the following periods in the intrauterine process of development: (A) prelabyrinthal, when the formation of the brain proceeds exclusively according to coded genetic programs; (B) the canal period, the passage of which is already influenced by nerve impulses arising in the receptor of the semicircular canals; (C) the canal-otolith period, passing also under the influence of nerve impulses from otolith receptors.

The main facts indicate such periodization. For example, the insufficiency of development, and moreover the complete non-excitability of the labyrinth are accompanied, as a rule, by various forms of underdevelopment of the brain up to the appearance of asymmetry of its spatial structures and of reversible congenital deformities (Belkin, 1958; Russkikh and Lebedev, 1955 et al.).

It is also known that normally in a 14 or 15 week old fetus the myelinization of nerve fibers of the posterior ampullas of the vertical canals has already been completed, as well as the myelinization of the horizontal canals. At that time the first movement of the fetus is noted. The appearance of these indications may be considered to be a completion of the prelabyrinthal period of intrauterine development. It is characteristic that the impulses from the labyrinth are not perceived passively. As a result of them, the fetus not only receives its first impressions of space, but also begins to influence its own position in it. At the beginning of the 20th week, the myelinization of fibers going to the vestibular nuclei from the round and oval sacculi of the otolith system is completed. At this time the fetus is still comparatively small; it freely floats and rotates in the perifetal fluid, collecting signals coming from the simicircular canals of the labyrinth. But beginning with the 20th to 24th week of intrauterine life, /306 movements of the fetus become more energetic, and by then the pregnant woman perceives them in the form of perfectly distinct pushes and internal rotations. These are the indications of the canal period of development and the beginning of the canal otolith period.

During this period the fetus, under its own rotation, more frequently turns its head, and in addition it maintains it in this position; i.e., due to the beginning of the action of the otolith system of the labyrinth, it begins to orient itself in the gravitational field.

The fixing of the fetus in head presentation is made possible by the circumstance that in this position, APC of its head proves to be located coaxially to the so-called anatomo-physiological center of the pregnant woman's pelvis, owing to which the labyrinth of the fetus receives maximum stimulation while the woman is walking. Head presentation enables optimum passage of the birth process.

The importance of motions in the various periods of pregnancy was indicated by the material we collected which included 507 placenta with umbilical cords. The majority of the umbilical cords contains from 15 to 16 loops, and the upper range of variations of this indicator of fetal behavior in the womb may extend to 37 loops on one umbilical cord.

A Single Stereotaxic Functional Zero Reference System for the Skull, Head and Central Nervous System of Man

Man usually applies extremely varied positions in relation to the field of gravitation and various inertial vectors. But this must not be the source of supplementary complications studying the problem of spatial orientation.

First of all, it is necessary to correctly consider the role which strict directiveness of gravitational field of Earth plays

in these questions. One of the basic indicators distinguishing man in the animal world, i.e., his upright posture, serves in the given case as the decisive factor. Strict orientation of the body according to the field of gravitation not only decisively determines the structure of the skeleton and muscle, but also has no less influence on the very fine structures distributed in the head of the peripheral receptors of orientation. From the concept of APC, the regularities of this influence are so essential that they permit us to question the introduction of a single functional zero reference system for the study of both morphological and of physiological aspects of the skull and cervical section of the spine, their muscle, blood and fluid dynamics of the brain, its internal architectonics and also the regularities of structure and function of the peripheral receptors of orientation.

The possibile indicators of localization of a straight line /307 (axis) *GJOZ* (Figure 94) on the cervical section of the spine and of the skull were discussed above.

The authors called this line the vertical axis of the spinal column in the region of the neck and skull. Although the introduction of this axis was based on the use of a small number of correspondences, of corresponding anthropometric indicators of cervical vertabrae and the occipital bone of the skull, nonetheless such a bold step should have somehow been strengthened, all the more so since the single reference system for the whole head introduced for the above-mentioned goals must be confirmed in all or almost all spheres of its investigation.

We will take the sphere of myology. Mastoid processes (*ms*) on the skull (Figs. 93 and 95) serve as the fundamental points of attachment of m. stenocleidomastoideus to it which are responsible for rotation of the head in the frontal plane *YOZ* around axis *OX*. Clearly this eccentricity of basic points of attachment of these muscles on the skull relative to its vertical axis would be inexpedient for a head, since this would elicit supplementary "pulsation" of the head in adjacent planes. Anthropometric investigations of the skull from this point of view indicate that the lower points on the mastoid processes actually are projected onto the proposed vertical axis (cf. *mf* in Fig. 95) *LImsOZ* were very high correlation coefficients. This even more strengthens the status of the given axis as a vertical one.

Now, naturally, a question arises as to the spatial orientation of any of the horizontals of the skull, i.e. a straight line, perpendicular to the axis *GOZ*. As far as the position of the possible points of their intersection is concerned, i.e. the level on which it would be most expedient to pass this horizontal line, then in the light of the given concept of APC it is natural to take for this point the nucleus of the APC region, point *O* (cf. Figs. 93, 94, 95 and 96). In addition it proves to be the case that if the head were oriented by rotations in the sagittal plane in such a way that

the centers of the condyles of the occipital bone were opposite the centers (2-2 in Fig. 95) of the platforms of contact on the atlas, then the straight line *OX* passing through the APC nucleus perpendicular to the vertical axis *OZ* will pass in the dorsal portion of a horizontal axis of symmetry of the upper and lower halves of the cerebellum and in the medial as the optical axis of both eyes.

These circumstances strengthen the status both of the vertical and the horizontal axes even more, which were thus introduced into the space of the human skull. They even serve as a basis for the /308 introduction of three-dimensional reference system beginning in nucleus *O* of the APC region within axis *OX* joined to the center of the pupil line (Fig. 94), with axis *OZ* going upwards and with axis *OY* going to the left (through the center of the sagittal canals of the labyrinth).

The functional zero reference system thus introduced contains in it definition in particular the horizontal zero plane *P* which may be taken as the zero functional horizontal plan for compiling stereotaxical charts of the human brain. This is very important. The fact of the matter is that to date the existing methods of compilation of stereotaxic charts relied on a random zero horizontal plan which was artificially taken approximately at 10 mm (for several types of animals) relative to the so-called basic plan. The basic plan rests on the orientations of the skull which do not bear almost any functional content mainly: the orion point (*or*) the lower edge of the left orbit of the eye and the two porion points (*po*) the upper points on the skull near the external acoustic meati (Fig. 95). In other words a zero and consequently, even basic, plan of construction on a Frankfort horizontal plane which, as is known, possesses the insufficiency that it does not appear as a physiological horizontal of the face and skull of man. It is characteristic that the necessity in the basic plan is because the zero plan having no relation to physiological horizontal, passes on too low a level in relation to the brain (the line *or-po*). Therefore the basic plan must be elevated with such an account that in its cross section several more masses of the brain matter appear than in the zero plane (Meshcherskiy, 1961). In addition, the localization on the skull of the basic plan intuitively approximates the localization of the introduced physiological horizontal plane. However from the position of the conception of the APX it is clear that such an approximation in quantitative relation, and intuitive in theoretical relation, construction of the original reference system for the investigation of brain cannot be proved. The original zero functional reference system must be based not on random support points of the skull but on functional kinematic parameters of the skull, the brain and its peripheral receptors of orientation.

We note, *apropos* of this, that at the basis of the introduced zero functional reference system there are, in particular, two basic peripheral receptors of orientation: visual and labyrinthal.

Actually in this system the basic horizontal physiological /309
P passes through the center of both eyes and the APC nucleus and consequently through the utricular regions of the labyrinth. Such correspondence is not random. In the first place, as is shown in experiments of I.C. Beritov (1961), the visual and labyrinth receptors are the fundamental peripheral receptors of orientation concentrated in the space of the skull; and in the second place, the position of the physiological horizontal, defined on the basis of these receptors, agrees with the premises discussed above on the basis of the physiological designations of the system of the occipito-atlantal articulations.

It was assumed above that the kinematic scheme of these articulations was intended chiefly for the creation of optimum conditions of orientation and, at the same time, we see that the physiological horizontal plane *P* is perpendicular to the earlier chosen vertical axis *OZ* with the condition of such distribution of the head on the spinal column, when the centers of the condyle are combined with the centers of the corresponding working surfaces of the atlas (Figs. 93, 94, 95 and 96).

The above described zero stereotaxic system probably may serve as a functional biological reference system in various spheres of investigation of the skull head and central nervous system of man.

Structural Functional Stereotaxic Bases of Labyrinthology

The labyrinth is located at the entrance into the cybernetic scheme of the system of the vestibular analyzer. The specifics for the differentiation of the signals which are excited in the labyrinth may be put at the basis of the study of the majority of questions and problems of labyrinthology. In addition, there is the view that all of these must be based on the same functionally justified reference system.

For the labyrinth this is especially important because the slightest nuances in localization and orientation of its separate structures in the volume of the body are reflected in its function. In this regard it is impossible to compare it with any other organ. This much is clear: insofar as the labyrinth is concerned, with the analysis of localization and orientation of the body in space, its particular localization and orientation within the volume of the body has decisive significance.

But with the investigation of the labyrinth in these positions it is necessary to have in the organism the functionally justified (in all spheres of activity of the organism) reference system to which also even the orientation of the labyrinth itself is subordinated. We consider the single stereotaxic functional malreference system as such a system, based on the concept of the APC of the head in central nervous system of man.

The human body at each given moment in time is oriented in space in relation to the surrounding objects, gravitational field and to the vector of inertia which acts on it in a definite way. In the volume of the human head, microstructures of the labyrinths are oriented in a definite way to the APC. Consequently in a structural, kinematic regard, the task of the labyrinth is, essentially, that it traces not changes in the spatial position of the man himself (which is too vastly complicated and unnecessary, but changes in relation to the inertial and gravitational position vectors and the space of the nucleus of its APC. /310

In this consists the logical mathematical clarity and simplicity of the construction of that physiological task which, at each given moment of orientation of man in space, is decided on the level of the functional activity of the labyrinth.

In this consists even the logical mathematical clarity and simplicity of the original orientation information which enters from the labyrinth into the vestibular nuclei located in the APC region.

Then, information on changes in the spatial position of the APC at the level of the cortical end of the vestibular analyzer is supplemented by the information arriving here from other peripheral receptors: visual, auditory, olfactory tactile and thermal (it is connected thereby with the position of surrounding objects), and being connected with the information arriving here in the form of cervical and trunk, tactile and tonic reflexes of position, it is extrapolated onto the spatial position of the body itself.

Thus, in the cybernetic system of analysis, on various stages of the central nervous system, the entrance of information from the labyrinth into it is the most important link in the entire complex of orientational information which is clear in a logico-mathematical sense.

This link appears still more important because it records in itself, each time, the original zero position of some reference system (in the given case, the original position of the APC region) in relation to which it carries on measurement of the new motion.

In the beginning of the preceding section we discussed the decisive role of the vertical position of man in the problems of his spatial orientation. For simplicity's sake, we will consider this position as the original one. In addition, the position of the head on the body is determined by localization on it of physiological horizontal plane P (Fig. 94). A three-dimensional zero reference system $XOYZ$ constructed on the basis of this plane, and the nucleus of the APC region bears with it three coordinate planes which have a concrete functional content for the orientational systems of the head.

The coordinate plane *XOY* (plane *P*) is the gravitational plane /311
of the APC. The gravitation vector to it is perpendicular and does not influence the motion in this plane with pure rotation of the head around the vertical axis *OZ* left or right. Owing to the fact that the optical centers of the eyes lie in the same plane, such rotations of the head, with the aim of collecting visual information at the level of the eyes, cannot elicit supplementary rotational motions of the latter in both orbits. Insofar as the majority of objects for the visual receptor are at eye-level, or are removed from it at a certain distance upward or downward from the plane *P*, then such localization in the volume of the head of the visual receptor is optimal for it. It is also characteristic that the cerebellum, which conducts the entire muscular sphere in its counteraction to the forces of gravitation, is located within the volume of the head in such a way that the gravitational plane *P* serves as a plane of symmetry of its upper and lower portion.

The coordinate plane *YOZ* (the frontal plane) functions as the inertial plane of the APC. Progressive motion, which begins from the position considered as original, is directed as a rule forward from this plane.

Therefore the vector of inertia is usually perpendicular to this plane. All structures located in this plane and in parallel to it are under the same dynamic conditions in relation to the action of such inertial vector.

The coordinate plane *XOZ* (sagittal) is the plane of bilateral symmetry or equilibrium. Lines in 19 analogous structures on the left and right sides are perpendicular to this plane.

This plane in which the two vectors considered above lie is gravitational and inertial, the combination of which forms the morphological structures of the skull of all representatives of the human phylogenetic order. Both labyrinths are subject to bilateral symmetry based on this plane. Moreover, they are intersected by the plane *YOZ* at the forward and rear portion by the gravitational plane *P* at the upper and lower portion. All these microstructures are subordinate to the central intersection of these three planes, i.e., the A structure of the APC. In addition they represent a certain analog of the APC structure, spaced from it along both sides of the plane of bilateral symmetry *XOZ*. Their task, according to the above hypothesis, consists of tracing the movement of the APC region in space, which has six degrees of freedom.

Each new APC position in space is calculated by the labyrinth by means of comparing it with the original which appears as the zero (reference) position. /312

Six degrees of freedom of spatial behavior of the APC determine the spatial structures of both labyrinths as six-pole triple field

mechanical transmitters. Three degrees of freedom of rotational movement of the APC are detected by the canals of both labyrinths. Three degrees of freedom of progressive motion of the APC are detected by the three otolith elements: reticular, sacculus and sacculusseca.

The mutual distributions of these microstructures in the labyrinth are characteristic. The neuroepithelium of each of the elements of the otolith system (17, 18, and 19) is perpendicular to the plane of the respective canal (14, 15 and 16) on the same side. Thus, in each pair, the otolith-canal represents the two poles of one dipole. It is responsible for rotation and progressive movements in the plane perpendicular to the dipole axis.

The mutual distribution of these structures in the opposite labyrinths is characteristic. Planes of the sagittal canals of these labyrinths are parallel to the visual paths of the eye of /313
the opposite side (we have in mind that with binocular vision in man, the visual paths intersect at a distance of the best vision, i.e. $\approx$ 30 cm). Planes of the frontal canals are parallel to the planes passing through the optical center of the opposite eyes perpendicular to their vision paths. Due to the higher coefficients of correlation between the spatial structures of a six-pole system of the canals of the labyrinth and the six-pole system of the ocularomotor muscles (8, 9, 10, 11, 12 and 13 in Fig. 94), the mechanism of nystagmus is easily accomplished.

The micro- and macro-structures of the labyrinth, represented by the APC concept, are expressions of the optimal condition of its functional activity in correspondence with the principle which was discussed above.

Excitation of signals in separate elements of the otolith and canal systems, the combination of these systems according to strength and sign, in particular, their complete absence in separate elements, depends in each concrete case on the plane in which rotation around the APC takes place or of progressive movement together with the APC.

The latter are differentiated according to the degree of synchronization (quantitative and sign function) of signals coming from both labyrinths to the APC.

This structural kinematic principle of optimality of the work of the labyrinth is accomplished by the principle of work optimality of the nucleic region itself of the APC. The latter amounts to the fact that all information enters from the APC into the remaining regions of the central nervous system, in particular the subcortex and the cortex of the brain, being synchronized in time: this takes place because the region of the APC is located equidistant from all lobes of the cortex and the subcortex. Insofar

as even the nerve substrata sending rhythmic synchronized time signals to the entire central nervous system is found in the APC region, then this principle of localization and action of the APC region may be called the principle of central spherical spatial temporal interrelations within the central nervous system.

Therefore even the cortex of the cerebellum, into which enter orientational signals from the APC region as well as from the center, is subordinate to this principle.

CONCLUSION

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Under terrestrial conditions, a large number of receptors (visual, auditory, vestibular, olfactory, tactile) and also proprioceptors of muscles and ligaments, and visceral proprioceptors may play an important role under definite conditions of orientation of higher vertebrate animals in space. But the visual and labyrinthal (semicircular canals and the vestibule of the inner ear) receptors have the greatest significance, insofar as with their exclusion normal orientation in space becomes impossible (Beritov 1961).

Orientation in space with closed eyes is accomplished more or less normally by means of some labyrinth receptors, i.e. with the participation of one vestibular analyzer and consequently without the direct participation not only of the olfactory, auditory and cutaneous analyzers but also with the direct participation of the motor analyzer (Beritov 1961).

The peripheral section of the vestibular analyzer, i.e. the vestibular apparatus consists of two portions: the otolith organs perceiving linear accelerations and the semi-circular canals perceiving angular accelerations. Such a division of the perception of two classes of accelerations is reflected in the mechanical characteristics of the moveable structures, the time constants of which differ by more than 300 times.

Despite a principle division of functions between the two subdivisions of the vestibular apparatus even at the level of sensory organs, there is interaction between the ampulla and otolith organs defined by the efferent system of the vestibular nerve.

The greatest portion of the vestibular afferent impulsation passes through the vestibular nuclei first to enter into the ascending or descending paths of the central nervous system. Several primary vestibular fibers pass the vestibular nuclei and are projected onto cells of the reticular formation of the cerebellum. The fact that the greater portion of the vestibular impulses passes through the vestibular nuclei does not signify that this relay station is a passive recipient and distributor of afferent signals already weakened and filtered by the efferent system of the vestibu-

lar nerve. The strategic position of the vestibular nuclei at the /315
beginning of the various vestibular reflex arcs testifies to the fact that they appear probably to be the most important station of the slave system. Here the flow of the vestibular impulses is controlled by tonic and phase central commands, and therefore the spatial and temporal model of impulsation is transformed, and the transmission "input-output" function essentially changes. Such a station of programming distribution of vestibular systems with the aid of neurons of the higher orders probably is a link of the greatest importance in the united and regulating activity, as a result of which the very best possible posture for motor reactions through any change of the external environment is performed.

The vestibular analyzer in the cortex of the cerebral hemispheres vary precisely and reacts diffentially to stimulation of the labyrinth receptors. It is capable of analyzing the slightest changes in the composition of stimulated labyrinth receptors and also changes in the direction and intensity of their stimulation (Beritov).

The vestibular analyzer is unique among the specialized sensory systems, due to the fact that its secondary fibers are extremely extensively distributed in the central nervous system. The branching of connections probably is a necessary characteristic of the sensory system whose chief function is the preservation of equilibrium and orientation of the animal in space. The threshold for the perception of angular acceleration in man is equal, on the average, to 1 $^{\circ}/sec^2$. The lowest value obtained from man is 0.2 $^{\circ}/sec^2$ (Clark, 1967). As was shown in Chapters II, III, and IV, sensitivity increases in a chain of receptors, i.e. neurons of the vestibular ganglion; neurons of the vestibular nuclei; neurons of the oculomotor nuclei.

The flow of vestibular impulses is progressively controlled by central command, and the spatial and temporal pattern of impulsation changes with the passage of each relay station corresponding with the modulating influence of the peripheral sensory mechanisms. Inhibitory central influences by means of the efferent system of the vestibular nuclei are performed at the level of receptors (Chapt. II); at the level of the vestibular nuclei /316
powerful inhibitory control is performed on the part of the cerebellum (Chapt. VI) in the spinal cord (Chapt. V).

Due to the scattering of the paths between the labyrinth and the cortex, anatomical investigations of the system descending and projecting into vestibular relay stations have not yet received sufficient illumination.

In all probability, in contrast to the somesthetic system with direct control connections to the first relay stations, the descending system from the cortex of the cerebral hemispheres to the vestibular nuclei has two or more synapses. For example, the

cortico-fugal fibers to the reticular formation from the sensory motor cortex of the parietal vestibular and occipital regions are well established, the reticular formation, in turn, is closely connected with vestibular nuclei. It was proved (Szentágothai, Rajkovits, 1958) that there are even direct corticofungal fibers to the vestibular nuclei. These fibers are scattered, which makes their dissection and evaluation of functional significance impossible. However the importance of monosynaptic and polysynaptic inhibitory corticofungal connections is unquestionable (Khilov, 1950).

What is the functional significance of the extremely low threshold for eliciting a flow of afferent vestibular impulsation in response to natural stimulation, when there is such a large number of inhibitory mechanisms controlling and damping the activity in all portions of the vestibular conducting system? One of the possible explanations is that tonic inhibitory influences weaken involuntary muscular contractions in response to weak, short-term vestibular stimuli. In the opposite case, involuntary muscular activity would hinder the completion of voluntary muscular activity (Gernandt, 1967).

Investigations during the last ten years of the process of synaptic transmission of excitation and inhibition in the central nervous system indicated an unusual complexity of the reflex organization. A detailed description of the structure of synoptic structures obtained by means of electron microscopy, demonstration of inhibitory and exciting synapses of electrical and chemical (with a great variety of mediators) transmission of a nerve impulse in them, and also the difference of electrical characteristics of most synaptic elements of dendrites, somas and axons of neurons give the possibility of evaluating the significance of these or other nerve connections anew. All this taken together created the necessary prerequisites for a special study of vestibular function. At the same time progress which has been achieved put forth a number of new complicated tasks awaiting their solution, namely: clarification of the functional significance of hair formations of the sensory cells; mechanisms of transformation of mechanical energy of an external stimulas into a nerve impulse; the significance of the efferent system of the vestibular nerve and forces of efferent control; definition of the functional significance of various types of reactions of neurons to adequate stimulation of vestibular apparatus; definition of the mediators and organization of synaptic structures in all connections of vestibular system; study of the /317 interaction with other analyzers and vegetative nervous system, without which the discovery of mechanisms of the pathogenesis of seasickness and development of unfavorable vegetative disturbances in weightlessness is impossible.

The avalanche-like increase in the number of investigations in the region of the study of the vestibular functions observed

in recent years allows us to hope that the combined forces of physiologists, morphologists, histochemists, biochemists, biophysicists and mathematicians will completely reveal the mechanisms of many vestibular reactions, and man will learn to direct them.

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